EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	393	(548/241).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/03/01 08:40
S2	2	("4172896").PN.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/03/01 09:02
S3	2	("6677458").PN.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/03/01 09:02

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 05	CASREACT(R) - Over 10 million reactions available
NEWS 4	DEC 14	2006 MeSH terms loaded in MEDLINE/LMEDLINE
NEWS 5	DEC 14	2006 MeSH terms loaded for MEDLINE file segment of TOXCENTER
NEWS 6	DEC 14	CA/CAplus to be enhanced with updated IPC codes
NEWS 7	DEC 21	IPC search and display fields enhanced in CA/CAplus with the IPC reform
NEWS 8	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 9	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 10	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 11	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 12	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 13	JAN 30	Saved answer limit increased
NEWS 14	JAN 31	Monthly current-awareness alert (SDI) frequency added to TULSA
NEWS 15	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 16	FEB 22	Status of current WO (PCT) information on STN
NEWS 17	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 18	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 19	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 20	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS 21	FEB 28	TOXCENTER reloaded with enhancements
NEWS 22	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data

NEWS EXPRESS	FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT http://download.cas.org/express/v8.0-Discover/
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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  * * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:08:51 ON 01 MAR 2006

=> fil reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                             ENTRY    SESSION
FULL ESTIMATED COST                                           0.21       0.21

FILE 'REGISTRY' ENTERED AT 10:09:27 ON 01 MAR 2006
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   27 FEB 2006  HIGHEST RN 875402-35-0
DICTIONARY FILE UPDATES:  27 FEB 2006  HIGHEST RN 875402-35-0

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

  Please note that search-term pricing does apply when
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**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\QUERIES\10662966.str
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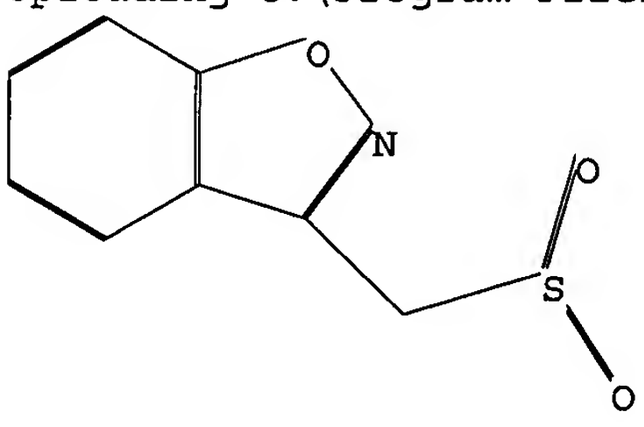

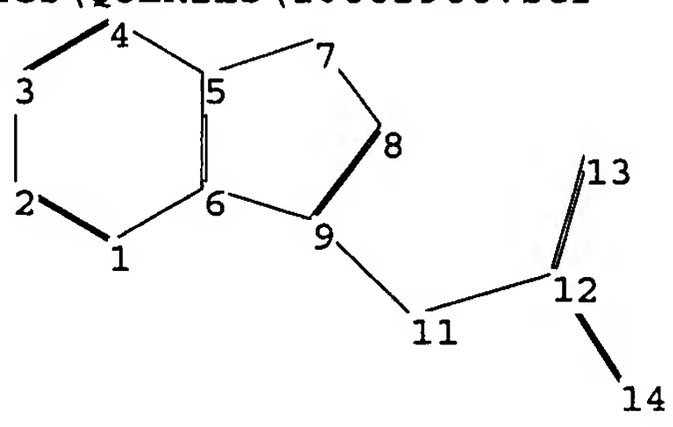


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chain nodes :
11  12  13  14
ring nodes :
1  2  3  4  5  6  7  8  9
chain bonds :
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ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  5-7  6-9  7-8  8-9
exact/norm bonds :
8-9  11-12  12-13  12-14
exact bonds :
5-7  6-9  7-8  9-11
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6
isolated ring systems :
containing 1 :


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  11:CLASS
12:CLASS  13:CLASS  14:CLASS

L1      STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1                STR
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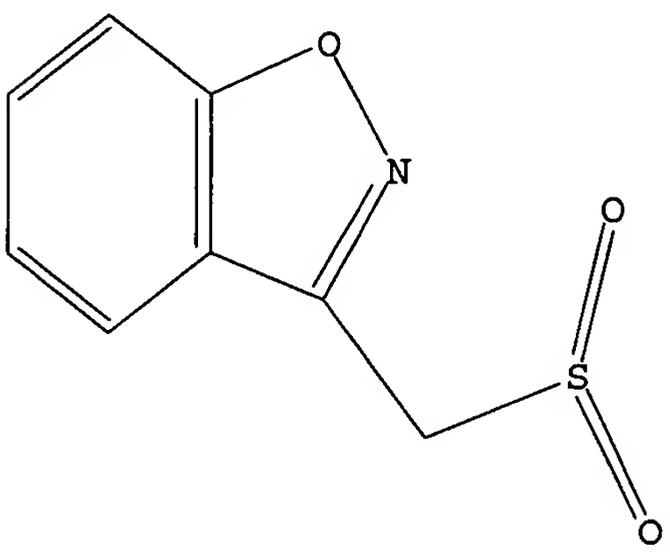


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Structure attributes must be viewed using STN Express query preparation.


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SAMPLE SEARCH INITIATED 10:09:48 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        7 TO ITERATE

100.0% PROCESSED         7 ITERATIONS                                 4 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            7 TO      298
PROJECTED ANSWERS:               4 TO      200

L2             4 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 10:09:51 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      146 TO ITERATE

100.0% PROCESSED      146 ITERATIONS                                85 ANSWERS
SEARCH TIME: 00.00.01

L3            85 SEA SSS FUL L1
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=> s l3 and caplus/lc
      49841738 CAPLUS/LC
L4           79 L3 AND CAPLUS/LC

=> s l3 not l4
L5            6 L3 NOT L4

=> d l5 1-6
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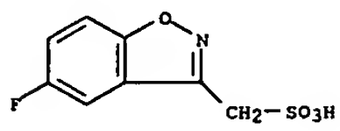
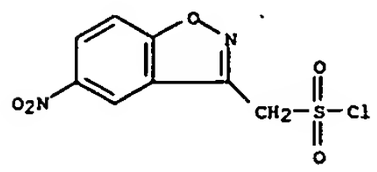
L5 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 774132-44-4 REGISTRY
ED Entered STN: 02 Nov 2004
CN 1,2-Benzisoxazole-3-methanesulfonic acid, 5-fluoro- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C8 H6 F N O4 S
CI COM
SR CA



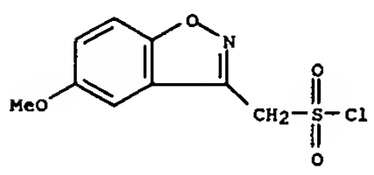
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L5 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 343323-97-7 REGISTRY
ED Entered STN: 26 Jun 2001
CN 1,2-Benzisoxazole-3-methanesulfonyl chloride, 5-nitro- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C8 H5 Cl N2 O5 S
SR Reaction Database
LC STN Files: CASREACT



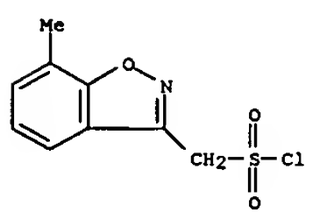
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L5 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 343319-77-7 REGISTRY
ED Entered STN: 26 Jun 2001
CN 1,2-Benzisoxazole-3-methanesulfonyl chloride, 5-methoxy- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C9 H8 Cl N O4 S
SR Reaction Database
LC STN Files: CASREACT



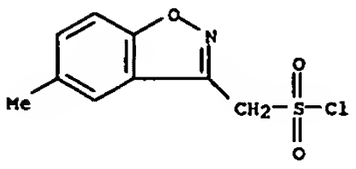
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L5 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 343317-91-9 REGISTRY
ED Entered STN: 26 Jun 2001
CN 1,2-Benzisoxazole-3-methanesulfonyl chloride, 7-methyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C9 H8 Cl N O3 S
SR Reaction Database
LC STN Files: CASREACT



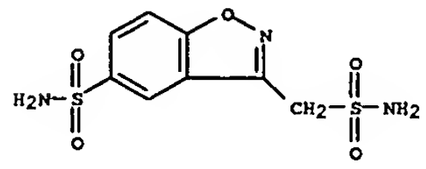
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L5 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 343317-48-6 REGISTRY
ED Entered STN: 26 Jun 2001
CN 1,2-Benzisoxazole-3-methanesulfonyl chloride, 5-methyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C9 H8 Cl N O3 S
SR Reaction Database
LC STN Files: CASREACT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L5 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 342805-32-7 REGISTRY
ED Entered STN: 21 Jun 2001
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-(aminosulfonyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C8 H9 N3 O5 S2
SR Reaction Database
LC STN Files: CASREACT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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=> fil caplus
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     183.54     183.75

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FILE COVERS 1907 - 1 Mar 2006  VOL 144 ISS 10
FILE LAST UPDATED: 28 Feb 2006  (20060228/ED)

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http://www.cas.org/infopolicy.html

=> d his

     (FILE 'HOME' ENTERED AT 10:08:51 ON 01 MAR 2006)

     FILE 'REGISTRY' ENTERED AT 10:09:27 ON 01 MAR 2006
L1                STRUCTURE UPLOADED
L2              4 S L1
L3             85 S L1 FULL
L4             79 S L3 AND CAPLUS/LC
L5              6 S L3 NOT L4

     FILE 'CAPLUS' ENTERED AT 10:10:29 ON 01 MAR 2006

=> s l4
L6            413 L4

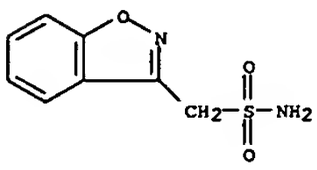
=> s l6 and sodium
          1021306 SODIUM
               34 SODIUMS
          1021315 SODIUM
                  (SODIUM OR SODIUMS)
L7             65 L6 AND SODIUM

=> d ibib abs hitstr 1-65
```

L7 ANSWER 1 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:103380 CAPLUS
TITLE: Compositions and methods for the treatment of disorders of the central and peripheral nervous systems
INVENTOR(S): Hochman, Daryl W.
PATENT ASSIGNEE(S): Cytoscan Sciences LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 101,000.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2006025387	A1	20060202	US 2005-130945		20050517
US 6495601	B1	20021217	US 1999-470637		19991222
US 2002082252	A1	20020627	US 2002-56528		20020123
US 2005267103	A1	20051201	US 2005-101000		20050407
PRIORITY APPLN. INFO.:			US 1998-113620P	P	19981223
			US 1999-470637	A2	19991222
			US 2001-263830P	P	20010123
			US 2002-56528	A2	20020123
			US 2005-101000	A2	20050407

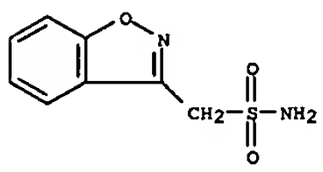
AB VThe present invention relates to methods and compns. for treating disorders of the central and/or peripheral nervous system by administering agents that are effective in reducing the effective amount, inactivating, and/or inhibiting the activity of a Na+-K+-2Cl (NKCC) cotransporter. In certain embodiments, the Na+-K+-2Cl- co-transporter is NKCC1.
IT 68291-97-4, Zonisamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for treatment of disorders of central and peripheral nervous systems)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



L7 ANSWER 2 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:100738 CAPLUS
TITLE: Novel dosage form comprising modified-release and immediate-release active ingredients
INVENTOR(S): Vaya, Navin; Karan, Rajesh Singh; Sadanand, Sunil; Gupta, Vinod Kumar
PATENT ASSIGNEE(S): India
SOURCE: U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of U.S. Ser. No. 630,446.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2006024365	A1	20060202	US 2005-134633		20050519
US 2004096499	A1	20040520	US 2003-630446		20030729
PRIORITY APPLN. INFO.:			IN 2002-MU697	A	20020805
			IN 2002-MU699	A	20020805
			IN 2003-MU80	A	20030122
			IN 2003-MU82	A	20030122
			US 2003-630446	A2	20030729

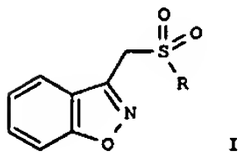
AB A dosage form comprising of a high dose, high solubility active ingredient as modified release and a low dose active ingredient as immediate release where the weight ratio of immediate release active ingredient and modified release active ingredient is from 1:10 to 1:15000 and the weight of modified release active ingredient per unit is from 500 mg to 1500 mg; a process for preparing the dosage form. Tablets containing 10 mg sodium pravastatin and 1000 mg niacin were prepared The release of sodium pravastatin after 24 h was 67.7%, and the release of niacin after 1 h was 84.1%.
IT 68291-97-4, Zonisamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



L7 ANSWER 3 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:33913 CAPLUS
DOCUMENT NUMBER: 144:128959
TITLE: Two crystalline forms of sodium 1,2-benzisoxazole-3-methanesulfonate, and processes for the preparation and use thereof in the synthesis of zonisamide
INVENTOR(S): Naddaka, Vladimir; Adin, Itai; Klopfer, Eyal; Arad, Oded; Kaspi, Joseph
PATENT ASSIGNEE(S): Israel
SOURCE: U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2006009644	A1	20060112	US 2005-153403		20050616
US 2006014814	A1	20060119	US 2005-153402		20050616
PRIORITY APPLN. INFO.:			US 2004-580360P	P	20040618
			US 2004-582086P	P	20040624
			US 2004-622009P	P	20041027

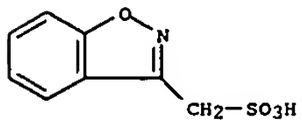
GI



I

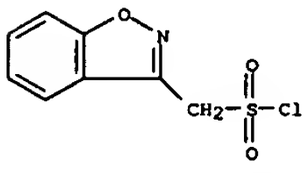
AB Disclosed is a process of preparing 1,2-benzisoxazole-3-methanesulfonamide (zonisamide). Also disclosed is (1) a method of dehydrating sodium 1,2-benzisoxazole-3-methanesulfonate monohydrate (I.H2O; R = ONa), a compound useful in the preparation of zonisamide (I; R = NH2), as well as (2) the crystalline forms of the dehydrated salt, sodium 1,2-benzisoxazole-3-methanesulfonate (I; R = ONa). The hydrate I.H2O (R = ONa) was prepared by sulfonylation of 3-(bromomethyl)-1,2-benzisoxazole with sodium sulfite. Compound I.H2O (R = ONa) was dehydrated by azeotropic distillation from toluene or toluene/DMF to give two crystalline forms of the dehydrated I, as determined by X-ray powder diffraction. Either form of dehydrated I (R = ONa) reacted with oxalyl chloride to give the corresponding sulfonyl chloride, which was treated in situ with ammonia to give zonisamide.
IT 73101-64-1P, Sodium 1,2-benzisoxazole-3-methanesulfonate

L7 ANSWER 3 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RL: IMF (Industrial manufacture); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cryst. forms of sodium 1,2-benzisoxazole-3-methanesulfonate and use in the synthesis of zonisamide)
RN 73101-64-1 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, sodium salt (9CI) (CA INDEX NAME)

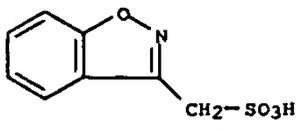


● Na

IT 73101-65-2P 81534-20-5P 342623-49-8DP, 1,2-Benzisoxazole-3-methanesulfonic acid, ester 342623-49-8P, 1,2-Benzisoxazole-3-methanesulfonic acid 501019-17-6P, Sodium 1,2-benzisoxazole-3-methanesulfonate monohydrate
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and crystalline forms of sodium 1,2-benzisoxazole-3-methanesulfonate and use in the synthesis of zonisamide)
RN 73101-65-2 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonyl chloride (9CI) (CA INDEX NAME)



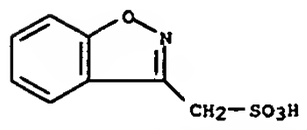
RN 81534-20-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, ammonium salt (9CI) (CA INDEX NAME)



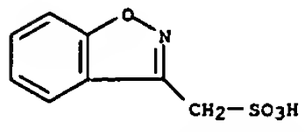
● NH_3

RN 342623-49-8 CAPLUS

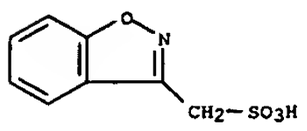
CN 1,2-Benzisoxazole-3-methanesulfonic acid (9CI) (CA INDEX NAME)



RN 342623-49-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid (9CI) (CA INDEX NAME)



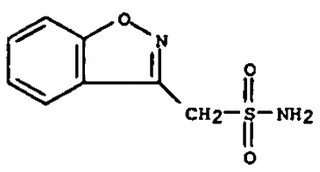
RN 501019-17-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, sodium salt, monohydrate (9CI) (CA INDEX NAME)



● Na

● H_2O

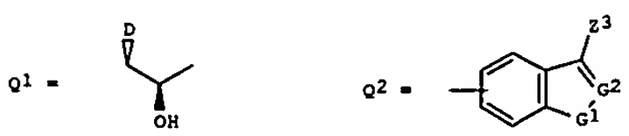
IT **68291-97-4P**, Zonisamide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation and crystalline forms of sodium 1,2-benzisoxazole-3-methanesulfonate and use in the synthesis of zonisamide)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2005:1240823 CAPLUS
DOCUMENT NUMBER: 144:6777
TITLE: Preparation of heterocyclyl sulfonylaminobenzylhydroxypropylcarbamates as HIV protease inhibitors
INVENTOR(S): Eissenstat, Michael; Delahanty, Greg; Topin, Andrey; Rajendran, Gnana Ravi
PATENT ASSIGNEE(S): Sequoia Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005110428	A2	20051124	WO 2005-US16056	20050509
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005267074	A1	20051201	US 2005-124056	20050509
PRIORITY APPLN. INFO.:			US 2004-568935P	P 20040507

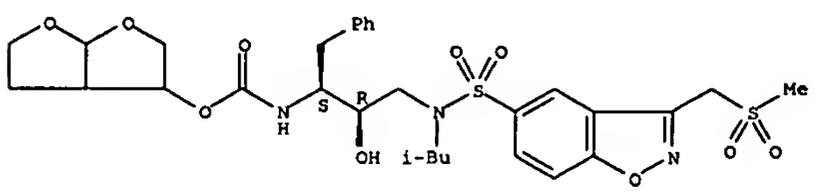
GI



AB XABA1X1 [X = (substituted) (fused) (bridged) 5-7 membered heterocyclyl containing ≥1 O, N, S, P; A = CONH, COCONH, SO2NH, etc.; B = Q1; D = (substituted) alkyl, alkenyl, alkynyl, aryl, cycloalkyl, aralkyl; A1 = ND1E1; D1 = (substituted) alkyl, alkenyl, alkynyl, aryl, cycloalkyl, aralkyl; E1 = CO, SO2; X1 = (substituted) Q2; G1 = NH, O; G2 = CZ2, N; Z2 = H, halo, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, etc.; Z3 = Z2, haloalkyl, etc.], were prepared Thus, (1-benzyl-2-hydroxy-3-isobutylaminopropyl)carbamic acid hexahydrofuro[2,3-b]furan-3-yl ester, benzofuran-5-sulfonyl chloride, and aqueous NaHCO3 were stirred together for 16 h in CH2Cl2 to give 98.5% [3-[(benzofuran-5-sulfonyl)isobutylamino]-1-benzyl-2-hydroxypropyl]carbamic acid hexahydrofuro[2,3-b]furan-3-yl ester. The latter showed a Ki = <0.10 nM.

IT **869988-76-1P 869988-96-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclyl sulfonylaminobenzylhydroxypropylcarbamates as HIV protease inhibitors)
RN 869988-76-1 CAPLUS
CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(2-methylpropyl)[[3-[(methylsulfonyl)methyl]-1,2-benzisoxazol-5-yl]sulfonyl]amino]-1-(phenylmethyl)propyl]-, hexahydrofuro[2,3-b]furan-3-yl ester (9CI) (CA INDEX NAME)

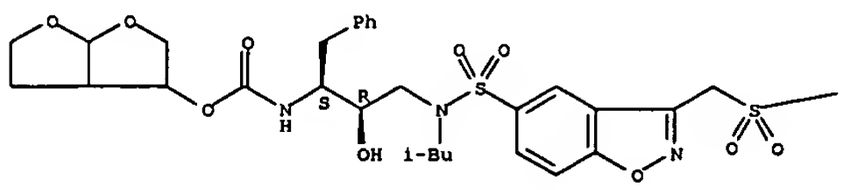
Absolute stereochemistry.



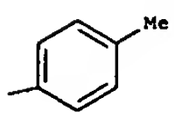
RN 869988-96-5 CAPLUS
CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[[[3-[[(4-methylphenyl)sulfonyl]methyl]-1,2-benzisoxazol-5-yl]sulfonyl](2-methylpropyl)amino]-1-(phenylmethyl)propyl]-, hexahydrofuro[2,3-b]furan-3-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L7 ANSWER 5 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1050940 CAPLUS
DOCUMENT NUMBER: 143:326350
TITLE: One-pot process for the preparation of 1,2-benzisoxazole-3-methanesulfonamide from 4-hydroxycoumarin
INVENTOR(S): Ueno, Yoshikazu; Ishikura, Tsutomu
PATENT ASSIGNEE(S): Japan
SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

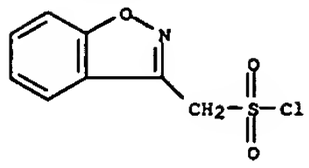
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005215796	A1	20050929	US 2005-88802	20050325
WO 2005092869	A1	20051006	WO 2005-JP5349	20050324

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

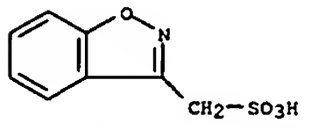
PRIORITY APPLN. INFO.: US 2004-556073P P 20040325

OTHER SOURCE(S): CASREACT 143:326350
AB 1,2-Benzisoxazole-3-methanesulfonamide was prepared by reaction of 4-hydroxycoumarin and NH2OH (salt) in H2O to give a mixture, acidification of the mixture and addition of ClCH2CH2Cl, removal of the aqueous layer to give a mixture containing 1,2-benzisoxazole-3-acetic acid and ClCH2CH2Cl, further removal of H2O by distillation, addition of ClSO3H, addition of base to give an alkali metal salt of 1,2-benzisoxazole-3-methanesulfonic acid, addition of POCl3 to give 1,2-benzisoxazole-3-methanesulfonyl chloride, and addition of NH3.
IT **73101-65-2P 342623-49-8DP**, 1,2-Benzisoxazole-3-methanesulfonic acid, alkali metal salt
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzisoxazolemethanesulfonamide from hydroxycoumarin)
RN 73101-65-2 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonyl chloride (9CI) (CA INDEX NAME)

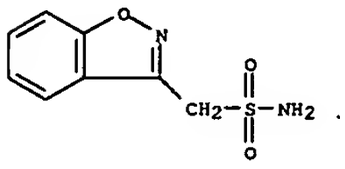
L7 ANSWER 5 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 342623-49-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid (9CI) (CA INDEX NAME)



IT **68291-97-4P**, 1,2-Benzisoxazole-3-methanesulfonamide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of benzisoxazolemethanesulfonamide from hydroxycoumarin)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



L7 ANSWER 6 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:962027 CAPLUS
DOCUMENT NUMBER: 143:235530
TITLE: Methods and compositions for the treatment of epilepsy, seizure disorders, and other CNS disorders
INVENTOR(S): Went, Gregory; Fultz, Timothy J.; Meyerson, Lawrence
PATENT ASSIGNEE(S): Neuromolecular, Inc., USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

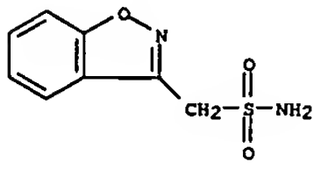
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005079773	A2	20050901	WO 2005-US4819	20050214
WO 2005079773	A3	20051027		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005245460	A1	20051103	US 2005-58141	20050214

PRIORITY APPLN. INFO.: US 2004-544839P P 20040213
US 2004-603903P P 20040824
US 2004-635786P P 20041213

AB The present invention relates to compns. comprising an NMDA receptor antagonists and an anti-epileptic drug for the treatment of CNS-related disorders. For example, tablets were formulated containing memantine 10, topiramate 30, dicalcium phosphate dihydrate 26.6, microcryst. cellulose 26.6, Na starch glycolate 1.2, Mg stearate 0.6, Eudragit RS30D 4.76, talc 3.3, and tri-Et citrate 0.95 mg per tablet.
IT **68291-97-4**, Zonisamide
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NMDA receptor antagonists and antiepileptics for treatment of CNS disorders)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

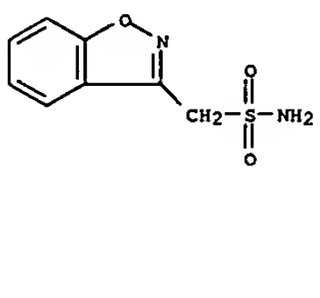


L7 ANSWER 6 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

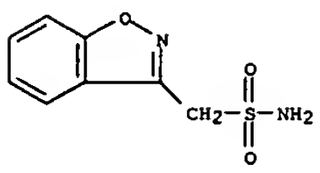
L7 ANSWER 7 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:624442 CAPLUS
DOCUMENT NUMBER: 143:206461
TITLE: Limbic neurotransmission reduction-based method for the treatment of clinical depression
INVENTOR(S): Binder, Michael Raymond
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 3 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005181071	A1	20050818	US 2005-58661		20050215
PRIORITY APPLN. INFO.:			US 2004-545223P	P	20040218
			US 2004-581627P	P	20040622

AB The invention is a new method for the treatment of clin. depression. The invention involves reducing neurotransmission in the limbic system of the human brain as a means of treating depressive symptoms.
IT **68291-97-4**, Zonisamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(limbic neurotransmission reduction-based method for treatment of clin. depression)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



L7 ANSWER 8 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



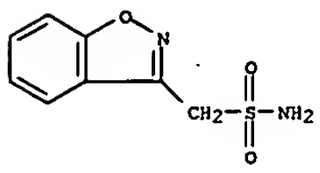
L7 ANSWER 8 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:611671 CAPLUS
DOCUMENT NUMBER: 143:126805
TITLE: Method of biochemical treatment of persistent pain by inhibiting biochemical mediators of inflammation
INVENTOR(S): Omoigui, Osemwota Sota
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 224,743.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005152905	A1	20050714	US 2005-58371		20050216
US 2004038874	A1	20040226	US 2002-224743		20020822
PRIORITY APPLN. INFO.:			US 2002-224743	A2	20020822

AB The invention discloses a method for the biochem. treatment of persistent pain disorders by inhibiting the biochem. mediators of inflammation in a subject, comprising administering to the subject any one of several combinations of components that are inhibitors of biochem. mediators of inflammation. The process for biochem. treatment of persistent pain disorders is based on Sota Omoigui's Law, which states: 'The origin of all pain is inflammation and the inflammatory response'. Sota Omoigui's Law of Pain unifies all pain syndromes as sharing a common origin of inflammation and the inflammatory response. The various biochem. mediators of inflammation are present in differing amts. in all pain syndromes and are responsible for the pain experience. Classification and treatment of pain syndromes should depend on the complex inflammatory profile. A variety of mediators are generated by tissue injury and inflammation. These include substances produced by damaged tissue, substances of vascular origin as well as substances released by nerve fibers themselves, sympathetic fibers and various immune cells. Biochem. mediators of inflammation that are targeted for inhibition include but are not limited to: prostaglandin, nitric oxide, tumor necrosis factor α, interleukin 1α, interleukin 1β, interleukin 4, Interleukin 6, and interleukin 8, histamine and serotonin, substance P, matrix metalloproteinase, calcitonin gene-related peptide, vasoactive intestinal peptide, as well as the potent inflammatory mediator peptide proteins neurokinin A, bradykinin, kallidin and T-kinin.
IT **68291-97-4**, Zonisamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biochem. treatment of persistent pain by inhibiting biochem. mediators of inflammation)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

L7 ANSWER 9 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:584881 CAPLUS
DOCUMENT NUMBER: 143:318281
TITLE: Lack of pharmacokinetic interactions between steady-state zonisamide and valproic acid in patients with epilepsy
AUTHOR(S): Ragueneau-Majlessi, Isabelle; Levy, Rene H.; Brodie, Martin; Smith, David; Shah, Jaymin; Grundy, John S.
CORPORATE SOURCE: Department of Pharmaceutics, University of Washington, Seattle, WA, USA
SOURCE: Clinical Pharmacokinetics (2005), 44(5), 517-523
CODEN: CPKNDH; ISSN: 0312-5963
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objectives: This study evaluated the effect of the addition of zonisamide on valproic acid (valproate sodium) pharmacokinetics under steady-state conditions in patients with epilepsy. A second aim was to characterize zonisamide pharmacokinetics in the presence of valproic acid. Methods: Twenty-two patients (males and females, 18-55 years of age) with their seizure disorder stabilized on valproic acid monotherapy were included in a two-center, open-label, one-way drug-interaction trial. The zonisamide dose was gradually increased from 100 mg/day to 400 mg/day. Three pharmacokinetic profiles were obtained: on days -7 and -1, to assess pharmacokinetic parameters of oral valproic acid administered alone, and on day 35, after 14 days of zonisamide treatment at the maximal tolerated dose, to evaluate the effect of zonisamide on valproic acid pharmacokinetics and to characterize zonisamide pharmacokinetics in the presence of valproic acid. Results: Seventeen patients completed the study, with 16 patients contributing to the pharmacokinetic analyses. Coadministration of zonisamide and valproic acid appeared reasonably well tolerated. Steady-state dosing of zonisamide (200mg twice daily) had no statistically significant effect on the mean (± SD) maximum observed plasma concentration (Cmax) [70.8 ± 20.5 vs 69.2 ± 27.0 μg/mL], area under the plasma concentration-time curve from the time of dosing to 12 h post-dose (AUC12) [689.3 ± 250.4 vs 661.8 ± 251.3 μg · h/mL] or other evaluated pharmacokinetic parameters for valproic acid measured before and after zonisamide administration. Furthermore, 90% confidence intervals for the ratio of the geometric means (day 35/day -1) of valproic acid pharmacokinetic exposure measures fell only slightly outside the 'no effect' range of 0.80-1.25. In the presence of valproic acid, mean zonisamide oral clearance (1.23 L/h) and elimination half-life (52.5 h) are generally consistent with values reported for healthy volunteers receiving zonisamide monotherapy. Conclusion: There is no apparent clin. significant effect of steady-state dosing of zonisamide on valproic acid pharmacokinetics, and valproic acid did not appear to affect the pharmacokinetics of zonisamide, indicating that no dosage adjustment of either drug should be required when they are used in combination in patients with epilepsy.
IT **68291-97-4**, Zonisamide
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zonisamide 400mg/day had no apparent clin. significant effect on

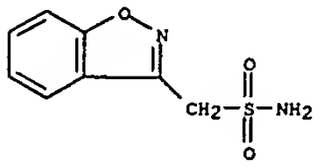
L7 ANSWER 9 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
valproic acid pharmacokinetics, no dosage adjustment is required in combination therapy, was well tolerated, safe with mild to moderate side effect in epileptic patient)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 10 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:485667 CAPLUS
DOCUMENT NUMBER: 143:165983
TITLE: Ligand-Based Virtual Screening and in Silico Design of
New Antimalarial Compounds Using Nonstochastic and Stochastic Total and Atom-Type Quadratic Maps
AUTHOR(S): Marrero-Ponce, Yovani; Iyarreta-Veitia, Maite; Montero-Torres, Alina; Romero-Zaldivar, Carlos; Brandt, Carlos A.; Avila, Priscilla E.; Kirchgatter, Karin; Machado, Yanetsy
CORPORATE SOURCE: Department of Pharmacy, Faculty of Chemical Pharmacy and Department of Drug Design, Chemical Bioactive Center, Central University of Las Villas, Santa Clara,
Villa Clara, 54830, Cuba
SOURCE: Journal of Chemical Information and Modeling (2005), 45(4), 1082-1100
CODEN: JCISD8; ISSN: 1549-9596
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Malaria has been one of the most significant public health problems for centuries. It affects many tropical and subtropical regions of the world.
The increasing resistance of Plasmodium spp. to existing therapies has heightened alarms about malaria in the international health community. Nowadays, there is a pressing need for identifying and developing new drug-based antimalarial therapies. In an effort to overcome this problem,
the main purpose of this study is to develop simple linear discriminant-based quant. structure-activity relation (QSAR) models for the classification and prediction of antimalarial activity using some of the TOMOCOMD-CARDD (TOpol. Mol. COMputer Design-Computer Aided "Rational" Drug Design) fingerprints, to enable computational screening from virtual combinatorial datasets. In this sense, a database of 1562 organic chems. having great structural variability, 597 of them antimalarial agents and 965 compds. having other clin. uses, was analyzed and presented as a helpful tool, not only for theor. chemists but also for other researchers in this area. This series of compds. was processed by a k-means cluster anal. to design training and predicting sets. Afterward, two linear classification functions were derived to discriminate between antimalarial
and nonantimalarial compds. The models (including nonstochastic and stochastic indexes) correctly classify more than 93% of the compound set, in
both training and external prediction datasets. They showed high Matthews' correlation coeffs., 0.889 and 0.866 for the training set and 0.855 and 0.857 for the test one. The models' predictivity was also assessed and validated by the random removal of 10% of the compds. to form
a new test set, for which predictions were made using the models. The overall means of the correct classification for this process (leave group 10% full-out cross validation) using the equations with nonstochastic and stochastic atom-based quadratic fingerprints were 93.93% and 92.77%, resp.
The quadratic maps-based TOMOCOMD-CARDD approach implemented in this work was successfully compared with four of the most useful models for antimalarials selection reported to date. The developed models were then used in a simulation of a virtual search for Ras FTase (FTase = farnesyltransferase) inhibitors with antimalarial activity; 70% and 100%

L7 ANSWER 10 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
of the 10 inhibitors used in this virtual search were correctly classified, showing the ability of the models to identify new lead antimalarials. Finally, these two QSAR models were used in the identification of previously unknown antimalarials. In this sense, three synthetic intermediaries of quinolinic compds. were evaluated as active/inactive ones using the developed models. The synthesis and biol. evaluation of these chems. against two malaria strains, using chloroquine as a ref., was performed. An accuracy of 100% with the theor. predictions
was obsd. Compd. 3 showed antimalarial activity, being the first report of an arylaminomethylenemalonate having such behavior. This result opens a door to a virtual study considering a higher variability of the structural core already evaluated, as well as of other chems. not included
in this study. We conclude that the approach described here seems to be a
promising QSAR tool for the mol. discovery of novel classes of antimalarial drugs, which may meet the dual challenges posed by drug-resistant parasites and the rapid progression of malaria illnesses.
IT 68291-97-4, Zonisamide
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ligand-based virtual screening and design of antimalarial compds.)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 111 THERE ARE 111 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

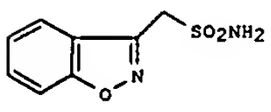
L7 ANSWER 11 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:429406 CAPLUS
DOCUMENT NUMBER: 142:482033
TITLE: A process for the manufacture of zonisamide, useful as
anticonvulsant agent
INVENTOR(S): Jaweed Mukarram, Siddiqui Mohammed; Merwade, Aravind Yehanathsa; Shukla, Jagdish Dattopant; Saiyad, Anis Mushtaqeali
PATENT ASSIGNEE(S): Wockhardt Limited, India
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005044808	A1	20050519	WO 2003-IB5052	20031111

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2003-IB5052 20031111

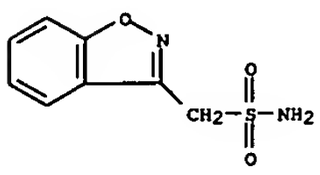
OTHER SOURCE(S): CASREACT 142:482033
GI



I

AB The invention relates to an improved process for the preparation of zonisamide
(I), a well known anticonvulsant. Other aspects of this invention are isolation of a key intermediate, viz., isolation of crystalline sodium chloride associated with 1,2-benzisoxazole-3-methane sodium sulfonate (BOS-Na:NaCl). Zonisamide (I, 99% HPLC purity) was prepared via
ring opening/cyclization of 4-hydroxycoumarin in the presence of NH2OH (step 1), sulfonation of the obtained 1,2-benzisoxazole-3-acetic acid, and
chlorination/amidation of the obtained sodium 1,2-benzisoxazole-3-methanesulfonate associated with NaCl (yield of step 1
was 95-98%). The anal. characteristics like IR and XRD data of BOS-Na:NaCl were also reported to confirm its nature.
IT 68291-97-4P, Zonisamide
RL: IMF (Industrial manufacture); PRP (Properties); PREP (Preparation)

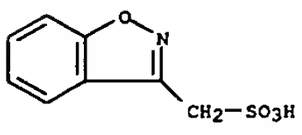
L7 ANSWER 11 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(process for the manuf. of zonisamide useful as anticonvulsant agent)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



IT **851961-40-5P**
RL: IMF (Industrial manufacture); PRP (Properties); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(process for the manufacture of zonisamide useful as anticonvulsant agent)
RN 851961-40-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, sodium salt, compd. with sodium chloride (NaCl) (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 342623-49-8
CMF C8 H7 N O4 S



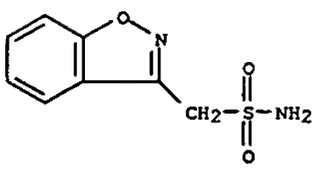
CM 2

CRN 7647-14-5
CMF Cl Na

Cl—Na

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 12 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

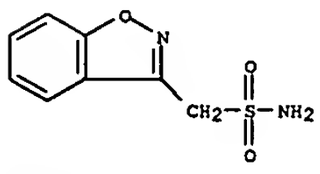


L7 ANSWER 12 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:369133 CAPLUS
DOCUMENT NUMBER: 142:435774
TITLE: Compositions treatment of chronic inflammatory diseases
INVENTOR(S): Shapiro, Howard K.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S. Ser. No. 610,073, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005090553	A1	20050428	US 2004-924945	20040824
PRIORITY APPLN. INFO.:			US 1992-906909	B2 19920630
			US 1994-241603	B2 19940511
			US 1997-814291	B2 19970310
			US 2000-610073	B2 20000705

OTHER SOURCE(S): MARPAT 142:435774
AB This invention defines novel compns. that can be used for clin. treatment of a class of chronic inflammatory diseases. Increased generation of carbonyl substances, aldehydes and ketones, occurs at sites of chronic inflammation and is common to the etiologies of all of the clin. disorders addressed herein. Such carbonyl substances are cytotoxic and addnl. serve to perpetuate and disseminate the inflammatory process. This invention defines use of compns., the orally administered required primary agents of which are primary amine derivs. of benzoic acid capable of reacting with the carbonyl substances. P-Aminobenzoic acid (or PABA) is an example of the required primary agent of the present invention. PABA has a small mol. weight, is water soluble, has a primary amine group which reacts with carbonyl-containing substances and is tolerated by the body in relatively high dosages for extended periods. The method of the present invention includes administration of a composition comprising: (1) an orally consumed primary agent; (2) a previously known medicament co-agent recognized as effective to treat a chronic inflammatory disease addressed herein administered to the mammalian subject via the oral route, other systemic routes of administration or via the topical route; and (3) optionally 1 or more addnl. orally consumed co-agent selected from the group consisting of antioxidants, vitamins, metabolites at risk of depletion, sulfhydryl co-agents, co-agents which may facilitate glutathione activity and nonabsorbable primary amine polymeric co-agents, so as to produce an additive or synergistic physiol. effect of an anti-inflammatory nature.
IT **68291-97-4**, Zonisamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. treatment of chronic inflammatory diseases)

L7 ANSWER 13 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:180322 CAPLUS
DOCUMENT NUMBER: 143:53301
TITLE: Synthesis of aryl semicarbazones as potential anticonvulsant agents
AUTHOR(S): Yogeeswari, P.; Sriram, D.; Veena, V.; Kavya, R.; Rakhra, K.; Ragavendran, J. Vaigunda; Mehta, S.; Thirumurugan, R.; Stables, J. P.
CORPORATE SOURCE: Medicinal Chemistry Research Laboratory, Pharmacy Group, Birla Institute of Technology and Science, Pilani, 333031, India
SOURCE: Biomedicine & Pharmacotherapy (2005), 59(1-2), 51-55
CODEN: BIPHEX; ISSN: 0753-3322
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of 4-ethoxyphenyl semicarbazones have been synthesized using an appropriate synthetic route and characterized by elemental analyses and spectral data. The anticonvulsant activity of all the synthesized compds. was evaluated against maximal electroshock induced seizures (MES) and s.c. pentylenetetrazole (scPTZ) induced seizure models in mice. The neurotoxicity was assessed using the rotorod method. All the test compds. were administered at doses of 30, 100, and 300 mg/kg body weight and the anticonvulsant activity was noted at 0.5 and 4 h time intervals after the drug administration. Among the compds. some tested, compds. showed protection from seizures in both the animal models. Some compds. were found to increase γ-aminobutyric acid (GABA) levels in the medulla oblongata region of the rat brain.
IT **68291-97-4**, Zonisamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis of aryl semicarbazones as potential anticonvulsant agents)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

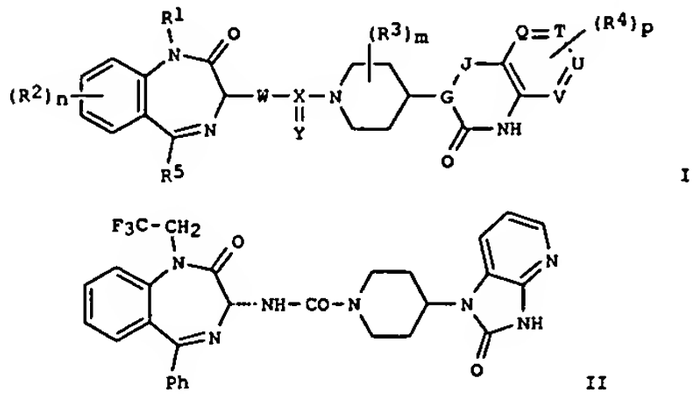
L7 ANSWER 14 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:136493 CAPLUS
DOCUMENT NUMBER: 142:240471
TITLE: Preparation of benzodiazepine derivatives as CGRP receptor antagonists
INVENTOR(S): Burgey, Christopher S.; Stump, Craig A.; Williams, Theresa M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005013894	A2	20050217	WO 2004-US20209	20040624

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-482854P P 20030626

OTHER SOURCE(S): MARPAT 142:240471
GI

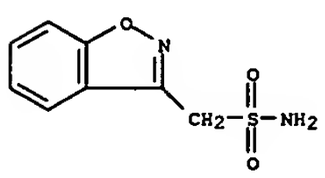


I

II

AB Benzodiazepine derivs. of formula I [R1 = H, alkyl, cycloalkyl, aryl, etc.; R2 = H, alkyl, cycloalkyl, aryl, etc.; R3 = H, alkyl, CO2H, alkoxycarbonyl; R4 = H, alkyl, cycloalkyl, aryl, etc.; R5 = H, alkyl,

L7 ANSWER 14 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
cycloalkyl, etc.; n = 1-4; m = 1-9; p = 1-4; W = O, (substituted) NH, (substituted) CH2; X = C, S; Y = O, NCONH2, etc.; G, J = N, NCH2, etc.;
Q,
T, U, V = CH, N; with provisos] are prepd. as antagonists of CGRP receptors, and are useful in the treatment or prevention of diseases in which the CGRP is involved, such as headache, migraine and cluster headache. The invention is also directed to pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which CGRP is involved.
Thus,
II was prepd. in several steps. The prepd. compds. had IC50 values < 50 μM against CGRP receptor.
IT 68291-97-4, Zonisamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic agent for co-administration with benzodiazepines)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



L7 ANSWER 15 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:14369 CAPLUS
DOCUMENT NUMBER: 142:114110
TITLE: Preparation of benzodiazepine CGRP receptor antagonists
INVENTOR(S): Burgey, Christopher S.; Stump, Craig A.; Williams, Theresa M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000807	A2	20050106	WO 2004-US20206	20040624
WO 2005000807	A3	20050106		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2529227	AA	20050106	CA 2004-2529227	20040624

PRIORITY APPLN. INFO.: US 2003-482674P P 20030626
WO 2004-US20206 W 20040624

OTHER SOURCE(S): MARPAT 142:114110
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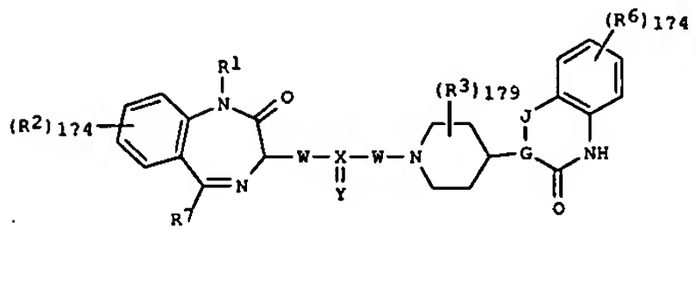

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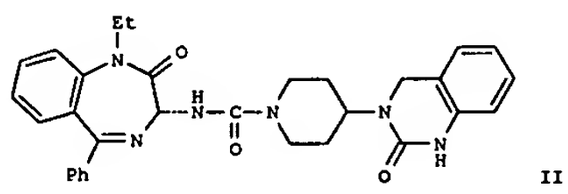
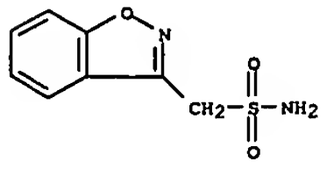


II

AB Title compds. I [R1 = H, alk(en/yn)yl, etc.; R2 = H, alkyl, cycloalkyl, etc.; R7 = H, alk(en/yn)yl, etc.; W = O, amino, alkyl; X = C, S; Y = O, NCN, etc.; R3 = H, alkyl, CN, etc.; R6 = H, alkyl, cycloalkyl, etc.; G-J =
N, N-alkyl, etc.] are prepared for instance, II is prepared from (R)-3-amino-1-ethyl-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepine oxalate, p-nitrophenylchloroformate and 3-(piperidin-4-yl)-3,4-dihydroquinazolin-2(1H)-one hydrochloride. Compds. I exhibit affinity for
the CGRP receptor with an IC50 of less than 50μM. I, alone or in combination with other agents, are useful for the treatment of diseases in
which the CGRP is involved, such as headache, migraine and cluster headache.
IT 68291-97-4, Zonisamide
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of benzodiazepine CGRP receptor
antagonists for headaches)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



L7 ANSWER 15 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

L7 ANSWER 16 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1059117 CAPLUS
DOCUMENT NUMBER: 142:43770
TITLE: Carbostyril derivatives and mood stabilizers for treating mood disorders
INVENTOR(S): Kikuchi, Tetsuro; Iwamoto, Taro; Hirose, Tsuyoshi
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004105682	A2	20041209	WO 2004-US13308	20040519
WO 2004105682	A3	20050512		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2526562	AA	20041209	CA 2004-2526562	20040519
EP 1626721	A2	20060222	EP 2004-785621	20040519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

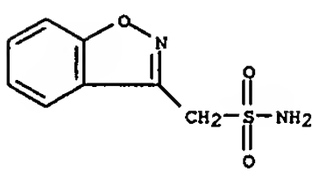
PRIORITY APPLN. INFO.: US 2003-473378P P 20030523
WO 2004-US13308 W 20040519

AB The pharmaceutical composition of the present invention comprises a carbostyril derivative which is a dopamine-serotonin system stabilizer and a mood stabilizer in a pharmaceutically acceptable carrier. The carbostyril derivative may be aripiprazole or a metabolite thereof. The mood stabilizer may include but is not limited to lithium, valproic acid, divalproex sodium, carbamazapine, oxcarbamazapine, zonisamide, lamotrigine, topiramate, gabapentin, levetiracetam or clonazepam. These compns. are used to treat patients with mood disorders, particularly bipolar disorder with or without psychotic features, mania or mixed episodes. Methods are provided for sep. administration of a carbostyril derivative and a mood stabilizer to a patient with a mood disorder. Thus, a formulation contained dehydroaripiprazole 5, clonazepam 600, starch 131, Mg stearate 4, and lactose 60 mg.

IT **68291-97-4**, Zonisamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carbostyril derivs. and mood stabilizers for treating mood disorders)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

L7 ANSWER 16 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



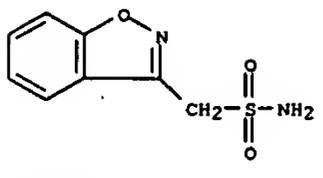
L7 ANSWER 17 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:966532 CAPLUS
DOCUMENT NUMBER: 142:290371
TITLE: Acute treatment of bipolar depression with adjunctive zonisamide: a retrospective chart review
AUTHOR(S): Baldassano, Claudia F.; Ghaemi, S. Nassir; Chang, Alice; Lyman, Alan; Lipari, Melissa
CORPORATE SOURCE: Bipolar Outpatient Program, University of Pennsylvania
School of Medicine, Philadelphia, PA, USA
SOURCE: Bipolar Disorders (2004), 6(5), 432-434
CODEN: BDIIAU; ISSN: 1398-5647
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB This retrospective chart review evaluated the use of zonisamide as adjunctive treatment in patients with bipolar depression. The charts of outpatients with bipolar I or II disorder treated with adjunctive zonisamide were reviewed. The efficacy of zonisamide was assessed via comparison of physician-rated Global Assessment of Functioning (GAF) and Clin. Global Impression of Severity (CGI-S) Scale scores at baseline and after 6 wk of therapy using paired t-tests. Patients who scored ≤2 on the CGI-S after 6 wk of zonisamide therapy were considered good responders to zonisamide. Charts for 12 patients (four men and eight women) with a mean (± SD) age of 39.6 (± 7.6) years were evaluated. Patients received a mean (± SD) zonisamide dosage of 236 (± 68) mg/day. Mean GAF scores significantly improved from 44.0 at baseline to 59.3 at week 6 ($P = 0.05$). Mean CGI-S scores improved from 4.54 at baseline to 3.42 at week 6, but the change was not statistically significant. Six patients (50.0%) were considered responders to zonisamide. Four patients discontinued zonisamide therapy, two for an adverse event (sedation) and two for lack of efficacy. Zonisamide may be a useful adjunctive treatment for some patients with bipolar depression. Conclusions from this study are limited due to its retrospective design. Further investigation of zonisamide in the treatment of bipolar depression is warranted.

IT **68291-97-4**, Zonisamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjunctive zonisamide in treatment of bipolar depression)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 18 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:965059 CAPLUS
DOCUMENT NUMBER: 141:406113
TITLE: Use of riluzole for the treatment of diseases characterized by hyperproliferation of keratinocytes in particular atopic dermatitis and psoriasis
INVENTOR(S): Sych, Michael; Goppelt, Andreas
PATENT ASSIGNEE(S): Switch Biotech A.-G., Germany
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096216	A2	20041111	WO 2004-EP4478	20040428
WO 2004096216	A3	20050414		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1477166	A1	20041117	EP 2003-9559	20030428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CA 2521152	AA	20041111	CA 2004-2521152	20040428
EP 1622614	A2	20060208	EP 2004-729853	20040428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

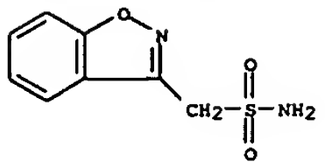
PRIORITY APPLN. INFO.:
EP 2003-9559 A 20030428
US 2003-471882P P 20030520
WO 2004-EP4478 W 20040428

AB The present invention relates to the use of Riluzole if needed with suitable adjuvants and additives for the production of a medicament for the treatment of diseases characterized by hyperproliferation of keratinocytes and/or T cells, in particular psoriasis and neurodermatitis as well as compns. comprising Riluzole and use thereof.

IT **68291-97-4**, Zonisamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(riluzole for the treatment of diseases characterized by hyperproliferation of keratinocytes in particular atopic dermatitis and psoriasis)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

L7 ANSWER 18 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L7 ANSWER 19 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:902155 CAPLUS
DOCUMENT NUMBER: 141:384286
TITLE: Novel encochleation methods, cochleates and methods of use
INVENTOR(S): Mannino, Raphael J.; Gould-Fogerite, Susan; Krause-Elsmore, Sara L.; Delmarre, David; Lu, Ruying
PATENT ASSIGNEE(S): Biodelivery Sciences International, Inc., USA; University of Medicine and Dentistry of New Jersey
SOURCE: PCT Int. Appl., 195 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091578	A2	20041028	WO 2004-US11026	20040409
WO 2004091578	C1	20050127		
WO 2004091578	A3	20050331		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005013854	A1	20050120	US 2004-822230	20040409
EP 1624858	A2	20060215	EP 2004-759375	20040409
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.:
US 2003-461483P P 20030409
US 2003-463076P P 20030415
US 2003-499247P P 20030828
US 2003-502557P P 20030911
US 2003-532755P P 20031224
US 2004-537252P P 20040115
US 2004-556192P P 20040324
WO 2004-US11026 W 20040409

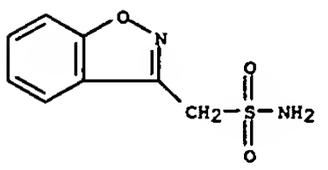
AB The invention generally relates to cochleate drug delivery vehicles. Disclose are novel methods for making cochleates and cochleate compns. that include introducing a cargo moiety to a liposome in the presence of a solvent. Also disclosed are cochleates and cochleate compns. that include an aggregation inhibitor, and optionally, a cargo moiety. Addnl., anhydrous

L7 ANSWER 19 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

cochleates that include a protonized cargo moiety, a divalent metal cation and a neg. charge lipid are disclosed. Methods of using the cochleate compns. of the invention, including methods of administration, are also disclosed.

IT **68291-97-4**, Zonisamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel encochleation methods and cochleates and methods of use for delivery of drugs and other agents using liposomes and aggregation inhibitors)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



L7 ANSWER 20 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:606452 CAPLUS
DOCUMENT NUMBER: 141:140420
TITLE: A process for the preparation of benzo[d]isoxazol-3-yl-methanesulfonic acid
INVENTOR(S): Razzetti, Gabriele; Mantegazza, Simone; Castaldi, Graziano; Allegrini, Pietro; Lucchini, Vittorio; Bologna, Alberto
PATENT ASSIGNEE(S): Dinamite Dipharma S.P.A., Italy
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004063173	A1	20040729	WO 2003-EP314919	20031224
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2512791	AA	20040729	CA 2003-2512791	20031224
EP 1581508	A1	20051005	EP 2003-795972	20031224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

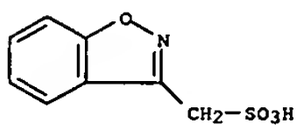
PRIORITY APPLN. INFO.: IT 2003-MI26 A 20030110
IT 2003-MI1383 A 20030704
WO 2003-EP14919 W 20031224

OTHER SOURCE(S): CASREACT 141:140420

AB The title compound (I) or its salt, useful as an intermediate in the preparation of anticonvulsant zonisamide, is prepared by reaction of 1,2-benzoxathin-4(3H)-one 2,2-dioxide oxime (II) with organic base or alkali or alkaline earth hydroxide. Thus, reaction of II with aq NaOH at room temperature for 3 h gave 70% sodium salt of I.

IT **726188-85-8P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of 1,2-benzisoxazole-3-methanesulfonic acid or its salt as intermediate for zonisamide)
RN 726188-85-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, compd. with N,N-diethylethanamine (1:1) (9CI) (CA INDEX NAME)

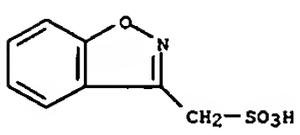
CM 1



CM 2

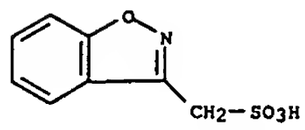
L7 ANSWER 20 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 726188-84-7 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, lithium salt (9CI) (CA INDEX NAME)



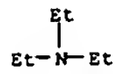
L7 ANSWER 20 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CRN 342623-49-8
CMF C8 H7 N O4 S

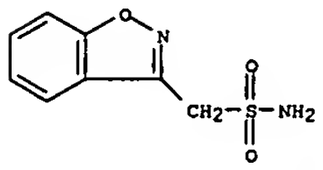


CM 2

CRN 121-44-8
CMF C6 H15 N



IT **68291-97-4P**, Zonisamide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(preparation of 1,2-benzisoxazole-3-methanesulfonic acid or its salt as intermediate for zonisamide)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



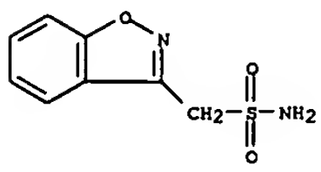
IT **73101-64-1P 726188-84-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1,2-benzisoxazole-3-methanesulfonic acid or its salt as intermediate for zonisamide)
RN 73101-64-1 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, sodium salt (9CI) (CA INDEX NAME)

L7 ANSWER 21 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:535729 CAPLUS
DOCUMENT NUMBER: 141:47215
TITLE: Antinociceptive effects of sodium channel-blocking agents on acute pain in mice
AUTHOR(S): Sakaue, Akiko; Honda, Motoko; Tanabe, Mitsuo; Ono, Hideki
CORPORATE SOURCE: Laboratory of CNS Pharmacology, Graduate School of Pharmaceutical Sciences, Nagoya City University, Nagoya, 467-8603, Japan
SOURCE: Journal of Pharmacological Sciences (Tokyo, Japan) (2004), 95(2), 181-188
CODEN: JPSTGJ; ISSN: 1347-8613
PUBLISHER: Japanese Pharmacological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of various sodium channel blocking agents on acute thermal and mech. nociception, as assessed using the plantar and tail pressure tests, resp., were compared with the effects of morphine. The drugs used were mexiletine, lidocaine, carbamazepine, phenytoin, eperisone, tolperisone, and zonisamide. The sodium channel blocking agents exhibited a rather preferential elevation of the threshold for thermal nociception. By contrast, morphine produced similar analgesic effects on thermal and mech. nociception. In the sciatic nerve isolated from mice, mexiletine, lidocaine, eperisone, and tolperisone impaired the propagation of low frequency action potentials (evoked at 0.2 Hz). Carbamazepine, phenytoin, and zonisamide generated a more frequency-dependent local anesthetic action with their obvious effects on higher frequency action potentials (evoked at 5 and/or 10 Hz). Our results show that sodium channel blocking agents have a preferential antinociceptive action against thermal stimulation that is likely to be attributed to their local anesthetic action.

IT **68291-97-4**, Zonisamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analgesic effects of sodium channel-blocking agents on acute pain in mice)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

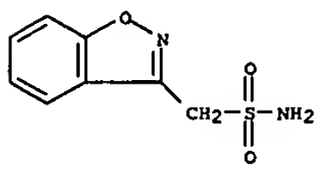


REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 22 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:506100 CAPLUS
DOCUMENT NUMBER: 141:167229
TITLE: Characterization of the anticonvulsant profile of valpromide derivatives
AUTHOR(S): Tasso, Silvina M.; Moon, Sung Ch.; Bruno-Blanch, Luis E.; Estiu, Guillermina L.
CORPORATE SOURCE: Medicinal Chemistry, Department of Biological Sciences, Facultad de Ciencias Exactas, Universidad Nacional de La Plata, La Plata, B1900AVV, Argent.
SOURCE: Bioorganic & Medicinal Chemistry (2004), 12(14), 3857-3869
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:167229

AB The antiepileptic activity of nine derivs. of valpromide is discussed. They comply with a pharmacophore model that establishes the essential structural and electronic features responsible for the protection against the MES test. The model results from the comparison of 17 structures, using d. functional methodologies combined with an active analog approach.
The derivs. of valpromide have been tested for anticonvulsant activity in mice. These compds. displayed a phenytoin-like profile, being active in the MES test and inactive in the PTZ test. 4-(Valproylamido)benzenesulfonamide is the most active compound, with an ED50 of 53 μmol/kg and no neurotoxicity at doses ≤1000 μmol/kg.
The pharmacol. behavior of the drugs points to a sodium channel blocking effect as one of the associated mechanisms. This mechanism was tested pos. for N-ethylvalpromide through its competition with the binding of [3H]batrachotoxin-A-20α-benzoate to the voltage-dependent sodium channels from rat brain synaptosomes.

IT 68291-97-4, Zonisamide
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of anticonvulsant profile of valpromide derivs. in relation to blocking voltage-dependent sodium channels and identification of pharmacophores of anticonvulsants)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:114301 CAPLUS
DOCUMENT NUMBER: 141:33256
TITLE: Comparison of Pharmacol. Properties of Rat NaV1.8 with Rat NaV1.2a and Human NaV1.5 Voltage-Gated Sodium Channel Subtypes Using a Membrane Potential Sensitive Dye and FLIPRR
AUTHOR(S): Vickery, R. G.; Amagasu, S. M.; Chang, R.; Mai, N.; Kaufman, E.; Martin, J.; Hembrador, J.; O'Keefe, M. D.; Gee, C.; Marquess, D.; Smith, J. A. M.
CORPORATE SOURCE: Theravance Inc., South San Francisco, CA, USA
SOURCE: Receptors and Channels (2004), 10(1), 11-23
CODEN: RCHAE4; ISSN: 1060-6823
PUBLISHER: Taylor & Francis, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel, membrane potential sensitive dye and a fluorescence imaging plate reader (FLIPRR) have been used to characterize the pharmacol. properties of rat Nav1.8 voltage-gated sodium channels (VGSC) in parallel with rat Nav1.2a and human Nav1.5 VGSC subtypes, resp. The sensitivity of recombinant Nav1.2a-CHO, Nav1.5-293-EBNA, and Nav1.8-F-11 cells to VGSC activators was subtype dependent. Veratridine evoked depolarization of Nav1.2a-CHO and Nav1.5-293-EBNA cells with pEC50 values of 4.78 ± 0.13 and 4.84 ± 0.12, resp. (n = 3), but had negligible effect on Nav1.8-F-11 cells (pEC50 < 4.5). Type I pyrethroids were without significant effect at all subtypes. In contrast, the type II pyrethroids deltamethrin and fenvalerate evoked direct depolarization of Nav1.8-F-11 and Nav1.5-293-EBNA cells. Deltamethrin potentiated the veratridine-evoked response in Nav1.8-F-11 cells by ≥20-fold, in contrast to a ≤3-fold potentiation of the response in Nav1.2a, and Nav1.5 cells. Tetrodotoxin (TTX) inhibited VGSC activator-evoked depolarization of Nav1.8-F-11 cells with a biphasic concentration-response curve.
The calculated pIC50 values were 8.05 ± 0.25 (n = 4) and 4.32 ± 0.21 (n = 4), corresponding to TTX inhibition of endogenous TTX-sensitive (TTX-S), and recombinant Nav1.8 TTX-resistant (TTX-R) VGSCs, resp. With the exception of TTX, the potencies of a number of ion channel blockers for the Nav1.8, Nav1.2a, and Nav1.5 VGSC subtypes were similar. In summary, these high-throughput FLIPRR assays represent a valuable tool for the determination of the relative potencies of compds. at different VGSC subtypes and may prove useful for the identification of novel subtype-selective inhibitors.

IT 68291-97-4, Zonisamide
RL: ANT (Analyte); ANST (Analytical study)
(comparison of pharmacol. properties of rat NaV1.8 with rat NaV1.2a and human NaV1.5 VGSC subtypes using membrane potential sensitive dye and FLIPRR)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

L7 ANSWER 24 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:41272 CAPLUS
DOCUMENT NUMBER: 140:99642
TITLE: Novel medicament combinations based on sodium channel blockers and magnesium salts
INVENTOR(S): Duettmann, Hermann; Weiser, Thomas
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004723	A1	20040115	WO 2003-EP6665	20030625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10230027	A1	20040122	DE 2002-10230027	20020704
CA 2491217	AA	20040115	CA 2003-2491217	20030625
AU 2003246582	A1	20040123	AU 2003-246582	20030625
EP 1521579	A1	20050413	EP 2003-762507	20030625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005532376	T2	20051027	JP 2004-518563	20030625
US 2004087513	A1	20040506	US 2003-612107	20030702

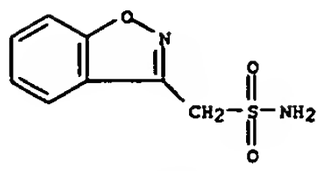
PRIORITY APPLN. INFO.: DE 2002-10230027 A 20020704
US 2002-408213P P 20020904
WO 2003-EP6665 W 20030625

OTHER SOURCE(S): MARPAT 140:99642

AB The invention relates to novel medicament combinations based on sodium channel blockers and magnesium salts. The invention also relates to a method for the production thereof and the use thereof in the production of medicaments for the treatment of ischemic states. The sodium channel blockers and magnesium salts are administered parenteral; magnesium salts can be administered orally. The two components can be included in sep. formulations or in one formulation. Thus a sodium channel blocker injection contained (mg): crobenetine hydrochloride 767; hydroxypropyl γ-cyclodextrin 10000; mannitol 11000; acetic acid (99%) 125.25; sodium acetate trihydrate 56.5; and water to 250 mL. A magnesium salt injection contained 1000 mg magnesium sulfate and 10 mL water.

IT 68291-97-4, Zonisamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicament combinations based on sodium channel blockers and magnesium salts)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

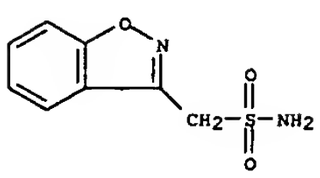
L7 ANSWER 24 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L7 ANSWER 25 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L7 ANSWER 25 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:1006769 CAPLUS
DOCUMENT NUMBER: 140:47530
TITLE: Medicament combinations of sodium channel blockers and fibrinolytics for treating ischemic conditions
INVENTOR(S): Banzet, Sophie; Duettmann, Hermann; Mauz, Annerose
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003105844	A1	20031224	WO 2003-EP5813	20030604
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10226814	A1	20040108	DE 2002-10226814	20020615
CA 2485751	AA	20031224	CA 2003-2485751	20030604
AU 2003250338	A1	20031231	AU 2003-250338	20030604
EP 1515720	A1	20050323	EP 2003-759907	20030604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005536478	T2	20051202	JP 2004-512748	20030604
US 2003235576	A1	20031225	US 2003-460709	20030612
PRIORITY APPLN. INFO.:			DE 2002-10226814 A	20020615
			US 2002-408144P P	20020904
			WO 2003-EP5813 W	20030604

OTHER SOURCE(S): MARPAT 140:47530

AB The invention relates to novel medicament combinations based on sodium channel blockers and fibrinolytics, to a method for producing the same and to the use thereof for producing medicaments for treating ischemic conditions. The selected sodium channel blockers and fibrinolytics can be prepared as one formulation or as two formulations. The synthesis of benzazocine compds. that are sodium channel blockers is described. An injection formulation containing the sodium channel blocker included: crobenetine hydrochloride 767 mg; hydroxypropyl γ-cyclodextrin 10000 mg; mannitol 11000 mg; acetic acid (99%) 125.25; sodium acetate trihydrate 56.6; water to 250 mL.

IT 68291-97-4, Zonisamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicament combinations of sodium channel blockers and fibrinolytics for treating ischemic conditions)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

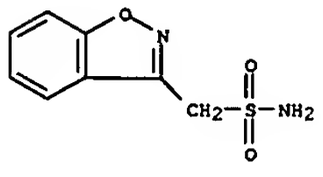
L7 ANSWER 26 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:985725 CAPLUS
DOCUMENT NUMBER: 140:12358
TITLE: Newer antiepileptic drugs: possible uses in the treatment of neuropathic pain and migraine
AUTHOR(S): Pappagallo, Marco
CORPORATE SOURCE: Division of Chronic Pain, Department of Pain and Palliative Medicine, Beth Israel Medical Center, New York, NY, USA
SOURCE: Clinical Therapeutics (2003), 25(10), 2506-2538
CODEN: CLTHDG; ISSN: 0149-2918
PUBLISHER: Excerpta Medica, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Background: Both neuropathic pain and migraine are now being treated with a variety of newer antiepileptic drugs (AEDs). The proven efficacy of gabapentin in postherpetic neuralgia (PHN) and painful diabetic neuropathy (PDN), and of divalproex sodium in the prevention of migraine has led to increased clin. investigation of the newer AEDs for these conditions. While basic and clin. research are expanding the knowledge base concerning the fundamental mechanisms of neuropathic pain and migraine, growing recognition of the similarities in the pathophysiol. of epilepsy, migraine, and various chronic pain disorders has further heightened interest in exploring the newer AEDs in the treatment of these conditions. Objective: The goals of this article were to review the empiric basis and scientific rationale for the use of AEDs in the treatment of neuropathic pain and migraine; summarize available clin. research on the use of 5 newer AEDs (gabapentin, lamotrigine, oxcarbazepine, topiramate, and zonisamide) in these conditions; and provide a summary comparison of the dosing, tolerability, and drug-interaction potential of these agents. Methods: Relevant English-language articles were identified through searches of MEDLINE (1990-Mar. 2003), American Academy of Neurol. abstrs. (1999-2003), and American Epilepsy Society abstrs. (2000-2002). The search terms were antiepileptic medication or drug, migraine headache, neuropathic pain, pathophysiol., treatment, mechanism of action, gabapentin, lamotrigine, oxcarbazepine, topiramate, and zonisamide. Conclusions: The newer AEDs possess the potential advantages of better tolerability and fewer drug-drug interactions compared with standard treatments such as tricyclic antidepressants or established AEDs. However, with the exception of data supporting the efficacy of gabapentin in PHN and PDN, there is currently insufficient evidence to determine whether the newer AEDs have equal or superior efficacy relative to proven pharmacotherapies.

IT 68291-97-4, Zonisamide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(newer antiepileptic drugs for treatment of neuropathic pain and migraine)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



L7 ANSWER 26 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

REFERENCE COUNT: 144 THERE ARE 144 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 27 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:777604 CAPLUS
DOCUMENT NUMBER: 139:271095
TITLE: Preemptive prophylaxis of migraine
INVENTOR(S): Cady, Roger K.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

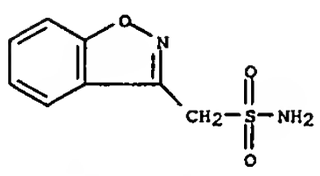
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080072	A1	20031002	WO 2003-US7993	20030314
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2479672	AA	20031002	CA 2003-2479672	20030314
AU 2003225813	A1	20031008	AU 2003-225813	20030314
PRIORITY APPLN. INFO.:			US 2002-365691P P	20020318
			WO 2003-US7993 W	20030314

AB A method of preventing the headache phase of migraine in a human comprises
administration of an anticonvulsant medication to said human exhibiting prodrome symptoms of migraine. Suitably, the method comprises administration of a migraine headache phase-preventing effective amount of
the anticonvulsant. There is also disclosed a pharmaceutical composition for
the prevention of the headache phase of a migraine containing an anticonvulsant as an active ingredient. There is also disclosed a method of determining prodromal symptoms of migraine using the following cognitive
tests: Simple Reaction Time (103); Running Memory Continuous Performance Task (104); Matching to Sample (105); Math. Processing Task (106); and interpreting the results as a percent of baseline indicator of need for prophylaxis.

IT **68291-97-4**, Zonisamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preemptive prophylaxis of migraine with anticonvulsant)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

L7 ANSWER 27 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

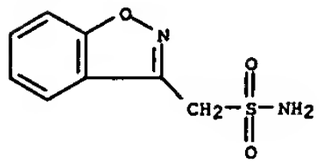
L7 ANSWER 28 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:760650 CAPLUS
DOCUMENT NUMBER: 140:104765
TITLE: Correlation between the physicochemical property of some nonsteroidal anti-inflammatory drugs and changes in adenosine triphosphate, glutathione and hemoglobin in rat erythrocytes
AUTHOR(S): Shimizu, Makiko; Tatsuno, Masahiro; Matsushita, Reiko;
Totsuka, Junko; Inoue, Yuko; Ohta, Kumiko; Kuniya, Kensuke; Fujii, Naomi; Fukasawa, Yoko; Watanabe, Nobuo; Iwata, Emiko; Miyazaki, Megumi; Hoshino, Makiko; Onda, Miho; Matsumura, Masae; Kikuchi, Yuichi;
Yamamoto, Chizuru; Hamada, Masashi; Tsuyuki, Aki; Furuta, Takashi; Kadokura, Chie; Kamiyama, Yoshimi; Kitahara, Goh; Suzuki, Kayoko; Sejima, Ei; Matsumoto, Yoshiaki; Fukuoka, Masamichi
CORPORATE SOURCE: Department of Clinical Pharmacology and Toxicology, Showa Pharmaceutical University, Tokyo, 194-8543, Japan
SOURCE: Biological & Pharmaceutical Bulletin (2003), 26(8), 1155-1165
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study was conducted to explore the relationship between physicochem. property and toxic effectiveness using rat red blood cells (RBCs). The toxic effectiveness of acid nonsteroidal anti-inflammatory drugs (NSAIDs) was systemically examined by the depletion of intracorpuscular ATP, glutathione (GSH), and Hb at various doses, increased every 5 fmol/RBC. When the RBCs were incubated with NSAIDs, the drugs attained maximum levels
within RBC, and the levels were then reduced. The ATP depletion seemed to
be observed on the excretion of the drugs prior to the depletions of GSH and
Hb. The physicochem. properties of NSAIDs were obtained from QMPRPlus, SMILES code, and CS ChemRaw Ultra. Correlation between their physicochem.
properties and their doses for the depletions of ATP, GSH and Hb was performed in comparison with those of the membrane bound enzyme (MBE) inhibiting- and metHb (MHb)-generating drugs. The ATP depletion by NSAIDs
was correlated with the GSH depletion and intracorpuscular levels of the drugs, but not with the Hb depletion. The GSH depletion was correlated with the Hb depletion and participated in the lipophilicity of the drugs.

IT **68291-97-4**, Zonisamide
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(correlation between NSAIDs physicochem. property and changes in ATP, glutathione, and Hb in erythrocytes)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



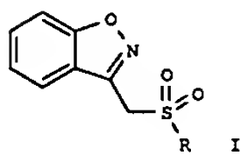
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

ACCESSION NUMBER: 2003:696874 CAPLUS
DOCUMENT NUMBER: 139:230763
TITLE: Method for preparing 1,2-benzisoxazole-3-methanesulfonyl chloride using thionyl chloride, and its amidation to form zonisamide
INVENTOR(S): Mendelovici, Marioara; Gershon, Neomi; Nidam, Tamar; Pilarski, Gideon; Sterinbaum, Greta
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072552	A1	20030904	WO 2003-US5690	20030224
WO 2003072552	C1	20040923		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475598	AA	20030904	CA 2003-2475598	20030224
AU 2003219889	A1	20030909	AU 2003-219889	20030224
US 2004014983	A1	20040122	US 2003-373554	20030224
US 6936720	B2	20050830		
EP 1472236	A1	20041103	EP 2003-716172	20030224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005526049	T2	20050902	JP 2003-571258	20030224
NO 2004003972	A	20040922	NO 2004-3972	20040922

PRIORITY APPLN. INFO.: US 2002-358916P P 20020222
WO 2003-US5690 W 20030224

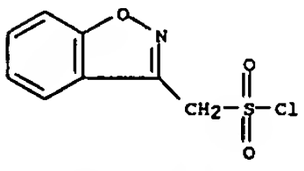
OTHER SOURCE(S): CASREACT 139:230763; MARPAT 139:230763
GI



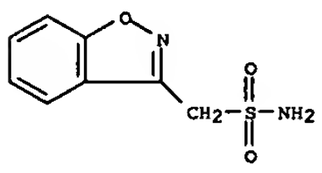
AB The invention relates to a process of preparing 1,2-benzisoxazole-3-

methanesulfonic acid chloride (I; R = Cl) (II). This compd. is useful as an intermediate for prepn. of the antiepileptic agent zonisamide (I; R = NH2) (III). II is prepd. via chlorination of the acid I (R = OH), or its salts or esters, using thionyl chloride (SOCl2). III is prepd. by amidation of II using NH3 in either aq., anhyd., or masked forms. More specifically, the invention provides a process of prepg. III, comprising the steps of : (1) chlorinating I (R = OH) or its salts or esters with SOCl2 in an org. solvent and/or in the presence of a catalyst to form II; and (2) amidating II in the presence of ammonia, the latter selected from the group consisting of (i) aq. ammonia in a biphasic system, (ii) masked ammonia, and (iii) dry ammonia, to form III. Use of SOCl2 to form the acid chloride avoids the use of POCl3, which is substantially more hazardous in the workplace. For instance, 4 equiv SOCl2 was added dropwise over 3 h to a mixt. of 1 equiv I (R = OH) Na salt in PhMe contg. 0.1 equiv DMF catalyst at 50-60°, followed by stirring at 50° for 4-5 h. Excess SOCl2 was removed by flowing N2, fresh PhMe was added, and inorg. salts were filtered to give a soln. of II in PhMe. This soln. was cooled to 10-15° and anhyd. NH3(g) was bubbled through the mixt. at that temp. until the reaction was complete. by HPLC. Filtration of inorg. salts, trituration with H2O at room temp., filtration, and washing with 95% EtOH gave crude III in 91.25% yield, contg. only 2.5% I.NH3 (R = OH) (IV) as an impurity. Recrystn. from refluxing 95% with active C treatment, filtration, and slow cooling, gave III in 90.8% yield with only 0.02% IV.

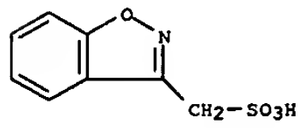
IT **73101-65-2P**, 1,2-Benzisoxazole-3-methanesulfonyl chloride
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of benzisoxazolemethanesulfonyl chloride using thionyl chloride, and its amidation to form zonisamide)
RN 73101-65-2 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonyl chloride (9CI) (CA INDEX NAME)



IT **68291-97-4P**, Zonisamide
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(product; preparation of benzisoxazolemethanesulfonyl chloride using thionyl chloride, and its amidation to form zonisamide)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

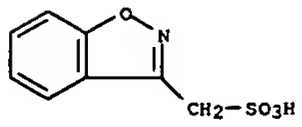


IT **73101-64-1**, 1,2-Benzisoxazole-3-methanesulfonic acid **sodium salt 81534-20-5**, Ammonium 1,2-benzisoxazole-3-methanesulfonate **342623-49-8**, 1,2-Benzisoxazole-3-methanesulfonic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of benzisoxazolemethanesulfonyl chloride using thionyl chloride, and its amidation to form zonisamide)
RN 73101-64-1 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, sodium salt (9CI) (CA INDEX NAME)



● Na

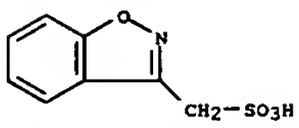
RN 81534-20-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, ammonium salt (9CI) (CA INDEX NAME)



● NH_3

RN 342623-49-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid (9CI) (CA INDEX NAME)

L7 ANSWER 29 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

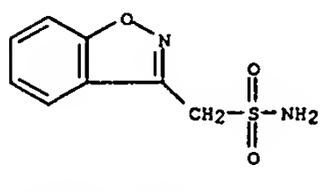
L7 ANSWER 30 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:535071 CAPLUS
DOCUMENT NUMBER: 139:286210
TITLE: Topological virtual screening: A way to find new anticonvulsant drugs from chemical diversity
AUTHOR(S): Bruno-Blanch, L.; Galvez, J.; Garcia-Domenech, R.
CORPORATE SOURCE: Faculty of Exact Sciences, Biological Sciences Department, Medicinal Chemistry Laboratory, National University of La Plata, La Plata, B1900AVV, Argent.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(16), 2749-2754
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A topol. virtual screening (tvs) test is presented, which is capable of identifying new drug leaders with anticonvulsant activity. Mol. structures of both anticonvulsant-active and non active compds., extracted from the Merck Index database, were represented using topol. indexes. By means of the application of a linear discriminant anal. to both sets of structures, a topol. anticonvulsant model (tam) was obtained, which defines a connectivity function. On the basis of this model, 41 new structures with anticonvulsant activity have been identified by a topol. virtual screening.

IT **68291-97-4**, Zonisamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topol. virtual screening to find new anticonvulsant drugs from chemical diversity)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L7 ANSWER 31 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:319495 CAPLUS
DOCUMENT NUMBER: 138:343864
TITLE: In vivo delivery methods and compositions
INVENTOR(S): Kensey, Kenneth
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 45 pp., Cont.-in-part of U.S. Ser. No. 819,924.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003078517	A1	20030424	US 2001-839785	20010420
US 6019735	A	20000201	US 1997-919906	19970828
CA 2301161	AA	19990304	CA 1998-2301161	19980826
NZ 502905	A	20010831	NZ 1998-502905	19980826
JP 2001514384	T2	20010911	JP 2000-507994	19980826
US 6322524	B1	20011127	US 1999-439795	19991112
US 6322525	B1	20011127	US 2000-501856	20000210
NO 2000000944	A	20000225	NO 2000-944	20000225
US 6428488	B1	20020806	US 2000-615340	20000712
WO 2002043806	A2	20020606	WO 2001-US44352	20011127
WO 2002043806	A3	20030327		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002026986	A5	20020611	AU 2002-26986	20011127
US 2002088953	A1	20020711	US 2001-33841	20011227
US 6624435	B2	20030923		
WO 2002079778	A2	20021010	WO 2002-US3984	20020207
WO 2002079778	A3	20030710		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002184941	A1	20021212	US 2002-156165	20020528
US 6571608	B2	20030603		

PRIORITY APPLN. INFO.:

US 1997-919906	A2	19970828
US 1999-439795	A2	19991112
US 2000-501856	A2	20000210
US 2000-628401	A2	20000801

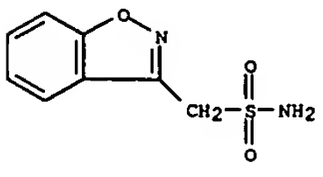
L7 ANSWER 31 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

US 2000-727950	B2	20001201
US 2001-819924	A2	20010328
US 1997-966076	A	19971107
WO 1998-US17657	W	19980826
US 2000-615340	A3	20000712
US 2000-228612P	P	20000828
US 2001-789350	B2	20010221
US 2001-828761	A	20010409
US 2001-839785	A	20010420
US 2001-841389	A	20010424
US 2001-897164	A3	20010702
WO 2001-US44352	W	20011127

AB Various methods are provided for determining and utilizing the viscosity of the circulating blood of a living being over a range of shear rates for diagnostics and treatment, such as detecting/reducing blood viscosity, work of the heart, contractility of the heart, for detecting/reducing the surface tension of the blood, for detecting plasma viscosity, for explaining/countering endothelial cell dysfunction, for providing high and low blood vessel wall shear stress data, red blood cell deformability data, lubricity of blood, and for treating different ailments such as peripheral arterial disease in combination with administering to a living being at least 1 drug. Agents effective to regulate at least 1 of the aforementioned blood parameters are used to adjust distribution of a substance through the bloodstream.

IT **68291-97-4**, Zonisamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vivo delivery methods and compns.)

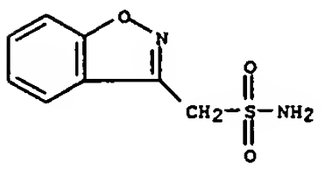
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



L7 ANSWER 32 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:280426 CAPLUS
DOCUMENT NUMBER: 139:63226
TITLE: Zonisamide for weight loss in obese adults. A randomized controlled trial
AUTHOR(S): Gadde, Kishore M.; Franciscy, Deborah M.; Wagner, H. Ryan, II; Krishnan, K. Ranga R.
CORPORATE SOURCE: Obesity Clinical Trials Program, Department of Psychiatry, Duke University Medical Center, Durham, NC, USA
SOURCE: JAMA, the Journal of the American Medical Association (2003), 289(14), 1820-1825
CODEN: JAMAAP; ISSN: 0098-7484
PUBLISHER: American Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Context: Zonisamide is a marketed antiepileptic drug that has serotonergic and dopaminergic activity in addition to blockade of sodium and calcium channels. Weight loss was an adverse effect associated with zonisamide treatment in epilepsy clin. trials. Objective: To evaluate the efficacy of zonisamide for weight loss in obese adults. Design and Setting: Sixteen-week randomized, double-blind, placebo-controlled trial with an optional single-blind extension of the same treatment for another 16 wk, conducted at Duke University Medical Center from Mar. 2001 to Mar. 2002. Participants: Fifty-five (92%) women and 5 (8%) men (mean [SE] body mass index, 36.3 [0.5]; mean age, 37.0 (1.0) years). Interventions: Patients were randomly assigned to receive zonisamide (n =30) or placebo (n=30). All participants were prescribed a balanced hypocaloric diet (500 kcal/d deficit) and compliance was monitored with self-rated food diaries. Zonisamide therapy was started at 100 mg/d orally, with gradual increase to 400 mg/d and further increase to 600 mg/d for patients losing less than 5% of body weight at the end of 12 wk. Placebo dosing was identical. Main Outcome Measure: Change in body weight Results: Of the 60 randomized patients, 51 completed the 16-wk acute phase. In an intent-to-treat anal. using the available data for all randomized participants with the last observation carried forward, the zonisamide group lost more body weight than the placebo group (mean [SE], 5.9 [0.8] kg [6.0% loss] vs. 0.9 [0.4] kg [1.0% loss]; t=5.5; P<.001) during the 16-wk period. A longitudinal mixed-model regression for weight change controlling for age, race, sex, body mass index, and percent body fat estimated that zonisamide treatment over the 16-wk study duration was associated with significantly greater weight loss than was placebo (t=6.4; P<.001). Seventeen (57%) of 30 in the zonisamide group and 3 (10%) of 30 in the placebo group lost at least 5% of body weight (P<.001) by week 16. Of the 37 participants who entered the extension phase, 36 completed week 32. The zonisamide group (n=19) had a mean weight loss of 9.2 kg (1.7 kg) (9.4% loss) at week 32 compared with 1.5 kg (0.7 kg) (1.8% loss) for the placebo group (n=17) (t=4.0; P<.001). Zonisamide was tolerated well, with few adverse effects. Conclusion: In this short-term, preliminary trial, zonisamide and hypocaloric diet resulted in more wt. loss than placebo and hypocaloric diet in the treatment of obesity.

IT 68291-97-4, Zonisamide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zonisamide for weight loss in obese adults)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 33 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:202630 CAPLUS
DOCUMENT NUMBER: 138:221579
TITLE: Process for the preparation of 1,2-benzisoxazole-3-methanesulfonic acid and its salts, intermediates in the synthesis of Zonisamide
INVENTOR(S): Nidam, Tamar; Mendelovici, Marioara; Schwartz, Eduard; Wizel, Shlomit
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020708	A1	20030313	WO 2002-US27593	20020829
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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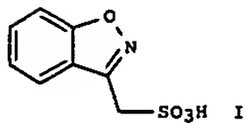
EP 1430037	A1	20040623	EP 2002-768748	20020829
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005506980	T2	20050310	JP 2003-524979	20020829

PRIORITY APPLN. INFO.: US 2001-316109P P 20010830
US 2001-344439P P 20011024
WO 2002-US27593 W 20020829

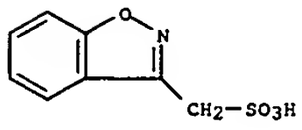
OTHER SOURCE(S): CASREACT 138:221579
GI



I

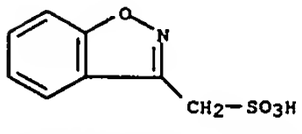
AB A process for the preparation of 1,2-benzisoxazole-3-methanesulfonic acid (I) by sulfonation of 1,2-benzisoxazole-3-acetic acid with chlorosulfonic acid or acyl sulfates in an org. solvent and optional conversion to its salts is disclosed. I has com. importance as a key intermediate in the prepn. of Zonisamide. For example, a soln. of 1,2-benzisoxazole-3-acetic acid (20 gm), 98% H2SO4 (22 gm), and Ac2O (23 gm) in AcOEt (80 mL) was heated at reflux for 4 h and the cooled reaction mixt. treated with aq. 10% aq. NaOH (120 mL) to give I•Na (20.33 gm) in 100% purity. Advantages of the present invention are: (1) the prepn. of I without the use of dioxane, improving the environmental safety of the reaction; and (2) the increased selectivity for prepn. of the monosulfonated over the bisulfonated benzisoxazole. Cryst. forms of 1,2-benzisoxazole-3-methanesulfonic acid (BOS-H) and its salts (BOS-Na, BOS-Ca, and BOS-Ba) were also characterized.

IT 73101-64-1P, 1,2-Benzisoxazole-3-methanesulfonic acid sodium salt 342623-49-8P, 1,2-Benzisoxazole-3-methanesulfonic acid 457635-27-7P, 1,2-Benzisoxazole-3-methanesulfonic acid calcium salt 457635-28-8P, 1,2-Benzisoxazole-3-methanesulfonic acid barium salt 501019-17-6P 501019-18-7P
RL: IMF (Industrial manufacture); PRP (Properties); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(target intermediate; preparation of benzisoxazolemethanesulfonic acid and salts, intermediates in the synthesis of Zonisamide, by sulfonation of benzisoxazoleacetic acid)
RN 73101-64-1 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, sodium salt (9CI) (CA INDEX NAME)



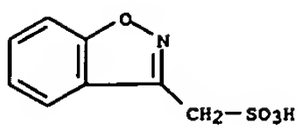
● Na

RN 342623-49-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid (9CI) (CA INDEX NAME)



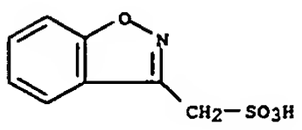
RN 457635-27-7 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, calcium salt (9CI) (CA INDEX NAME)

L7 ANSWER 33 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



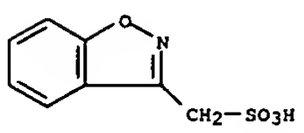
●1/2 Ca

RN 457635-28-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, barium salt (9CI) (CA INDEX NAME)



●1/2 Ba

RN 501019-17-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, sodium salt, monohydrate (9CI) (CA INDEX NAME)

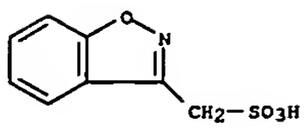


● Na

● H_2O

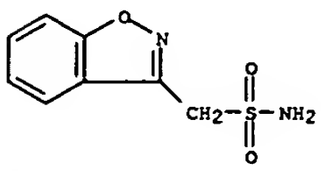
RN 501019-18-7 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, monohydrate (9CI) (CA INDEX NAME)

L7 ANSWER 33 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



● H_2O

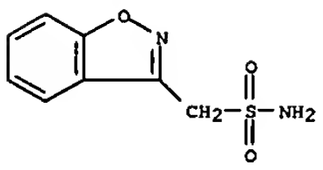
IT 68291-97-4P, Zonisamide
RL: IMF (Industrial manufacture); PREP (Preparation)
(target product; preparation of benzisoxazolemethanesulfonic acid and salts,
intermediates in the synthesis of Zonisamide, by sulfonation of benzisoxazoleacetic acid)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 34 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:33622 CAPLUS
DOCUMENT NUMBER: 139:143670
TITLE: Influence of various drugs on gastric emptying in rats
and the improving effects of mosapride citrate, a gastroprokinetic agent
AUTHOR(S): Yoshikawa, Takashi; Kawashima, Katsuyoshi; Yoshida, Naoyuki
CORPORATE SOURCE: Discovery Pharmacology II Group, Pharmacology and Microbiology Research, Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: Japanese Pharmacology & Therapeutics (2002), 30(11), 979-984
CODEN: JPTABU
PUBLISHER: Raifu Saiensu Shuppan K.K.
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Objective: Clin., some of the most common adverse effects induced by various drugs are gastrointestinal symptoms including anorexia, gastric pyrosis, epigastric pain, nausea and vomiting. However, the relation between gastrointestinal symptoms induced by drugs and dysfunction of gastric motility is unclear. In the present study, we investigated whether various drugs (zonisamide, pergolide mesilate, ibudilast, mexiletine hydrochloride, acarbose and sodium valproate), that have the gastrointestinal symptoms described above, delay gastric emptying in rats. Moreover, we investigated the effect of mosapride citrate, a gastroprokinetic agent, on the delay in gastric emptying induced by zonisamide and pergolide mesilate. Methods: The rats were fasted for 18 h before all expts. In the expts. for gastric emptying, test drugs or vehicle was orally administered 60 min before test meal (0.05% phenol red in 1.5% aqueous Me cellulose solution), which was given via a gastric tube (1.5 mL per animal). Fifteen minutes after administration of test meal, the stomach was removed and the amount of phenol red remaining in the stomach was measured. Results: Zonisamide, pergolide mesilate, ibudilast and mexiletine hydrochloride dose-dependently delayed gastric emptying in rats. However, acarbose and sodium valproate had no effect on gastric emptying. Mosapride citrate [0.1-3 mg/kg, p.o.] dose-dependently improved the delay in gastric emptying induced by zonisamide and pergolide mesilate. Conclusions: Delay in gastric emptying may be one of the important causes of gastrointestinal symptoms induced by various drugs. Moreover, gastroprokinetic agents, such as mosapride citrate, may be useful in improving drug induced gastrointestinal side effects.
IT 68291-97-4, Zonisamide
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(influence of various drugs on gastric emptying in rats and the improving effects of mosapride citrate, a gastroprokinetic agent)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

L7 ANSWER 34 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



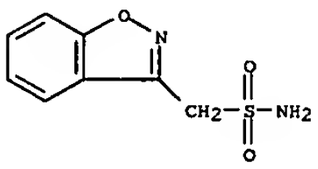
L7 ANSWER 35 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:913829 CAPLUS
DOCUMENT NUMBER: 139:769
TITLE: Exocytosis mechanism as a new targeting site for mechanisms of action of antiepileptic drugs
AUTHOR(S): Okada, Motohiro; Zhu, Gan; Yoshida, Shukuko; Kanai, Kazuaki; Hirose, Shinichi; Kaneko, Sunao
CORPORATE SOURCE: Department of Neuropsychiatry, Hirosaki University, Hirosaki, 036-8562, Japan
SOURCE: Life Sciences (2002), 72(4-5), 465-473
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Carbamazepine (CBZ) and zonisamide (ZNS) are effective antiepileptic drugs (AEDs) for the treatment of epilepsy and mood disorder. One of the mechanisms of action of CBZ and ZNS is inactivation of voltage-gated Na+ channel (VGSC). However, the major mechanism(s) of action of these AEDs is not clear yet. We have been exploring novel targeting mechanisms for the antiepileptic actions of CBZ and ZNS during the past ten years. In this report, we describe our hypothesis regarding the new targeting mechanisms for the antiepileptic action of AEDs. We determined an interaction between these AEDs and inhibitors of both voltage-sensitive Ca2+ channels (VSCCs) and soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) on neurotransmitter exocytosis using microdialysis. Perfusion with therapeutic concns. of CBZ and ZNS increased basal neurotransmitter release. This stimulatory action was predominantly inhibited by inhibitors of N-type VSCC and syntaxin. CBZ and ZNS increased Ca2+-evoked release, an action selectively inhibited by inhibitors of N-type VSCC and syntaxin. CBZ and ZNS reduced K+-evoked release, an action predominantly inhibited by inhibitors of P-type VSCCs and synaptobrevin. These actions of CBZ and ZNS on neurotransmitter exocytosis could be observed under the condition of inhibition of VGSC using perfusion with tetrodotoxin. Our findings enhance our understanding of the mechanisms of action of CBZ and ZNS as AEDs, which possibly reduce P-type VSCCs/synaptobrevin-related exocytosis mechanisms during the depolarization stage, and simultaneously enhance N-type VSCCs/syntaxin-related exocytosis mechanisms at the resting stage.

IT 68291-97-4, Zonisamide
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiepileptic drugs target neurotransmitter exocytosis mechanism)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 36 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:695963 CAPLUS
DOCUMENT NUMBER: 137:216942
TITLE: Process for the preparation of 1,2-benzisoxazole-3-acetic acid, an intermediate in the synthesis of zonisamide
INVENTOR(S): Mendelovici, Mariorara; Nidam, Tamar
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070495	A1	20020912	WO 2002-US6419	20020304
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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CA 2440030	AA	20020912	CA 2002-2440030	20020304
US 2002183525	A1	20021205	US 2002-90710	20020304
US 6677458	B2	20040113		
EP 1373229	A1	20040102	EP 2002-717527	20020304
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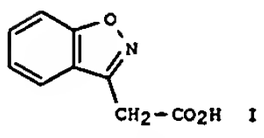
US 2004049053	A1	20040311	US 2003-661109	20030912

PRIORITY APPLN. INFO.: US 2001-273172P P 20010302
US 2001-294847P P 20010531
US 2002-90710 A3 20020304
WO 2002-US6419 W 20020304

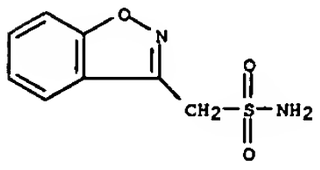
OTHER SOURCE(S): CASREACT 137:216942
GI



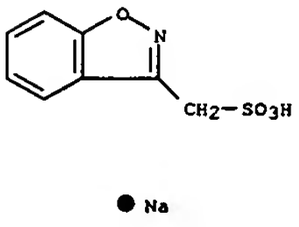
AB A process for the prepareation of 1,2-benzisoxazole-3-acetic acid (I) from 4-hydroxycoumarin and hydroxylamine.HCl in the presence of a base is disclosed. Compd. I has com. importance as a key intermediate in the prepn. of Zonisamide. For example, a soln. of 4-hydroxycoumarin (100 g), hydroxylamine hydrochloride (150 g) and diethylamine (160 g) in MeOH (500 mL) was heated at reflux for 1 h. The reaction mixt. was evapd. to dryness and the solid dissolved in aq. NaHCO3 and extd. with ether. After acidification of the aq. phase, the product was isolated by filtration, washed with water and dried to provide I (99.82 g) in 93 % wt./wt. yield. Avantages of the present invention are: (1) the prep. of I without the use of metallic sodium; and (2) the minimization of reaction side-products, e.g., oxime. The process is thus substantially less hazardous than previous methods. The invention also claims the prep. I or salts of which are converted to 1,2-benzisoxazole-3-methanesulfonamide, i.e., zonisamide.

IT 68291-97-4P, 1,2-Benzisoxazole-3-methanesulfonamide
73101-64-1P, 1,2-Benzisoxazole-3-methanesulfonic acid sodium salt 342623-49-8P, 1,2-Benzisoxazole-3-methanesulfonic acid 457635-27-7P 457635-28-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(product; process for preparation of 1,2-benzisoxazole-3-acetic acid, an intermediate in synthesis of zonisamide)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

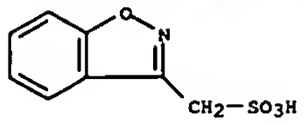


RN 73101-64-1 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, sodium salt (9CI) (CA INDEX NAME)

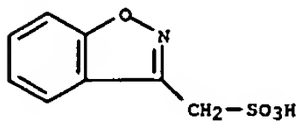


RN 342623-49-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid (9CI) (CA INDEX NAME)

L7 ANSWER 36 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

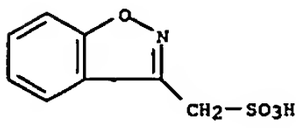


RN 457635-27-7 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, calcium salt (9CI) (CA INDEX NAME)



●1/2 Ca

RN 457635-28-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, barium salt (9CI) (CA INDEX NAME)



●1/2 Ba

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L7 ANSWER 37 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:428760 CAPLUS
DOCUMENT NUMBER: 137:24314
TITLE: Methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and treatment
INVENTOR(S): Kensey, Kenneth; Hokanson, Charles
PATENT ASSIGNEE(S): Visco Technologies, Inc., USA; Rheologics, Inc.
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002043806	A2	20020606	WO 2001-US44352	20011127
WO 2002043806	A3	20030327		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2301161	AA	19990304	CA 1998-2301161	19980826
NZ 502905	A	20010831	NZ 1998-502905	19980826
JP 2001514384	T2	20010911	JP 2000-507994	19980826
NO 2000000944	A	20000225	NO 2000-944	20000225
US 2002061835	A1	20020523	US 2001-828761	20010409
US 2003078517	A1	20030424	US 2001-839785	20010420
AU 2002026986	A5	20020611	AU 2002-26986	20011127

PRIORITY APPLN. INFO.:

US 1997-966076	A	19971107
US 2000-727950	A	20001201
US 2001-819924	A	20010328
US 2001-828761	A	20010409
US 2001-839785	A	20010420
US 1997-919906	A	19970828
WO 1998-US17657	W	19980826
US 1999-439795	A2	19991112
US 2000-501856	A2	20000210
US 2000-628401	A2	20000801
WO 2001-US44352	W	20011127

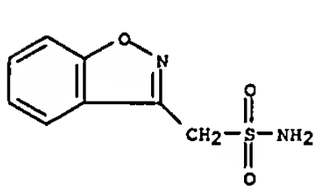
AB Various methods are provided for determining and utilizing the viscosity of the circulating blood of a living being over a range of shear rates for

L7 ANSWER 37 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

diagnostics and treatment, such as detecting/reducing blood viscosity, work of the heart, contractility of the heart, for detecting/reducing the surface tension of the blood, for detecting plasma viscosity, for explaining/countering endothelial cell dysfunction, for providing high and low blood vessel wall shear stress data, red blood cell deformability data, lubricity of blood, and for treating different ailments such as peripheral arterial disease in combination with administering to a living being at least one pharmaceutically acceptable agent. Agents pharmaceutically effective to regulate at least one of the aforementioned blood parameters are used to adjust distribution of a substance through the bloodstream.

IT **68291-97-4**, Zonisamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and treatment)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



L7 ANSWER 38 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:392219 CAPLUS
DOCUMENT NUMBER: 136:406945
TITLE: Methods for in vivo drug delivery based on monitoring blood flow parameters
INVENTOR(S): Kensey, Kenneth R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 727,950.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002061835	A1	20020523	US 2001-828761	20010409
US 6019735	A	20000201	US 1997-919906	19970828
CA 2301161	AA	19990304	CA 1998-2301161	19980826
NZ 502905	A	20010831	NZ 1998-502905	19980826
JP 2001514384	T2	20010911	JP 2000-507994	19980826
US 6322524	B1	20011127	US 1999-439795	19991112
US 6322525	B1	20011127	US 2000-501856	20000210
NO 2000000944	A	20000225	NO 2000-944	20000225
US 6428488	B1	20020806	US 2000-615340	20000712
WO 2002043806	A2	20020606	WO 2001-US44352	20011127
WO 2002043806	A3	20030327		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002026986	A5	20020611	AU 2002-26986	20011127
US 2002088953	A1	20020711	US 2001-33841	20011227
US 6624435	B2	20030923		
WO 2002079778	A2	20021010	WO 2002-US3984	20020207
WO 2002079778	A3	20030710		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF; BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002184941	A1	20021212	US 2002-156165	20020528
US 6571608	B2	20030603		

PRIORITY APPLN. INFO.:

US 1997-919906	A2	19970828
US 1999-439795	A2	19991112
US 2000-501856	A2	20000210

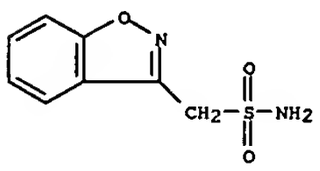
L7 ANSWER 38 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

US 2000-628401	A2	20000801
US 2000-727950	A2	20001201
US 1997-966076	A	19971107
WO 1998-US17657	W	19980826
US 2000-615340	A3	20000712
US 2000-228612P	P	20000828
US 2001-789350	B2	20010221
US 2001-819924	A	20010328
US 2001-828761	A	20010409
US 2001-839785	A	20010420
US 2001-841389	A	20010424
US 2001-897164	A3	20010702
WO 2001-US44352	W	20011127

AB Various methods are provided for determining and utilizing the viscosity of the circulating blood of a living being over a range of shear rates for diagnostics and treatment, such as detecting/reducing blood viscosity, work of the heart, contractility of the heart, for detecting/reducing the surface tension of the blood, for detecting plasma viscosity, for explaining/countering endothelial cell dysfunction, for providing high and low blood vessel wall shear stress data, red blood cell deformability data, lubricity of blood, and for treating different ailments such as peripheral arterial disease in combination with administering to a living being at least one pharmaceutically acceptable agent. Agents pharmaceutically effective to regulate at least one of the aforementioned blood parameters are used to adjust distribution of a substance through the bloodstream.

IT **68291-97-4**, Zonisamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for in vivo drug delivery based on monitoring blood flow parameters)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



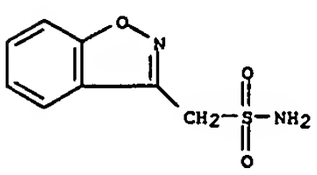
L7 ANSWER 39 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

US 2000-615340	A3	20000712
US 2000-228612P	P	20000828
US 2001-789350	B2	20010221
US 2001-828761	A	20010409
US 2001-839785	A	20010420
US 2001-841389	A	20010424
US 2001-897164	A3	20010702

AB Various methods are provided for determining and utilizing the viscosity of the circulating blood of a living being, i.e., a human, over a range of shear rates for diagnostics and treatment, such as detecting/reducing blood viscosity, work of the heart, contractility of the heart, for detecting/reducing the surface tension of the blood, for detecting plasma viscosity, for explaining/countering endothelial cell dysfunction, for providing high and low blood vessel wall shear stress data, red blood cell deformability data, lubricity of blood, and for treating different ailments such as peripheral arterial disease in combination with administering to a living being at least one pharmaceutically acceptable agent. Agents pharmaceutically effective to regulate at least one of the aforementioned blood parameters are used to adjust distribution of a substance through the bloodstream. For example, when blood viscosity is a blood flow parameter monitored, an agent is selected from i.v. diluents, red blood cell deformability agents, antiurea agents, oral contraceptives, antidiabetic agents, antiarrhythmics, antihypertensives, antihyperlipidemics, antiplatelet agents, appetite suppressants, antiobesity agents, blood modifiers, smoking deterrent agents, and nutritional supplements.

IT **68291-97-4**, Zonisamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(apparatus and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



L7 ANSWER 39 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:185688 CAPLUS
DOCUMENT NUMBER: 136:252567
TITLE: Methods for drug administration and distribution based on monitoring blood viscosity and other parameters for diagnostics and treatment
INVENTOR(S): Kensey, Kenneth
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 819,924.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002032149	A1	20020314	US 2001-841389	20010424
US 6019735	A	20000201	US 1997-919906	19970828
CA 2301161	AA	19990304	CA 1998-2301161	19980826
NZ 502905	A	20010831	NZ 1998-502905	19980826
JP 2001514384	T2	20010911	JP 2000-507994	19980826
US 6322524	B1	20011127	US 1999-439795	19991112
US 6322525	B1	20011127	US 2000-501856	20000210
NO 2000000944	A	20000225	NO 2000-944	20000225
US 6428488	B1	20020806	US 2000-615340	20000712
US 2002088953	A1	20020711	US 2001-33841	20011227
US 6624435	B2	20030923		
WO 2002079778	A2	20021010	WO 2002-US3984	20020207
WO 2002079778	A3	20030710		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002184941	A1	20021212	US 2002-156165	20020528
US 6571608	B2	20030603		

PRIORITY APPLN. INFO.:

US 1997-919906	A2	19970828
US 1999-439795	A2	19991112
US 2000-501856	A2	20000210
US 2000-628401	A2	20000801
US 2000-727950	A2	20001201
US 2001-819924	A2	20010328
US 1997-966076	A	19971107
WO 1998-US17657	W	19980826

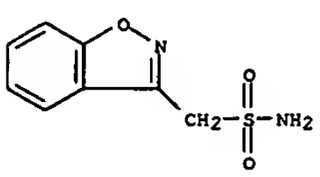
L7 ANSWER 40 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:384 CAPLUS
DOCUMENT NUMBER: 136:210464
TITLE: Randomized controlled trial of zonisamide for the treatment of refractory partial-onset seizures
AUTHOR(S): Faught, E.; Ayala, R.; Montouris, G. G.; Leppik, I. E.
CORPORATE SOURCE: Zonisamide 922 Trial Group, University of Alabama School of Medicine, Birmingham, UK
SOURCE: Neurology (2001), 57(10), 1774-1779
CODEN: NEURAI; ISSN: 0028-3878
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Zonisamide is a sulfonamide antiepilepsy drug with sodium and calcium channel-blocking actions. Experience in Japan and a previous European double-blind study have demonstrated its efficacy against partial-onset seizures. A randomized, double-blind, placebo-controlled trial enrolling 203 patients was conducted at 20 United States sites to assess zonisamide efficacy and dose response as adjunctive therapy for refractory partial-onset seizures. Zonisamide dosages were elevated by 100 mg/d each week. The study design allowed parallel comparisons with placebo for three dosages and a final crossover to 400 mg/d of zonisamide for all patients. The primary efficacy comparison was change in seizure frequency from a 4-wk placebo baseline to weeks 8 through 12 on blinded therapy. At 400 mg/d, zonisamide reduced the median frequency of all seizures by 40.5% from baseline, compared with a 9% reduction ($p = 0.0009$) with placebo treatment, and produced a ≥50% seizure reduction (responder rate) in 42% of patients. A dosage of 100 mg/d produced a 20.5% reduction in median seizure frequency ($p = 0.038$ compared with placebo) and a dosage of 200 mg/d produced a 24.7% reduction in median seizure frequency ($p = 0.004$ compared with placebo). Dropouts from adverse events (10%) did not differ from placebo (8.2%, NS). The only adverse event differing significantly from placebo was weight loss, though somnolence, anorexia, and ataxia were slightly more common with zonisamide treatment. Serum zonisamide concns. rose with increasing dose. Zonisamide is effective and well tolerated as an adjunctive agent for refractory partial-onset seizures. The minimal effective dosage was 100 mg/d, but 400 mg/d was the most effective dosage.

IT **68291-97-4**, Zonisamide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zonisamide for treatment of refractory partial-onset seizures)

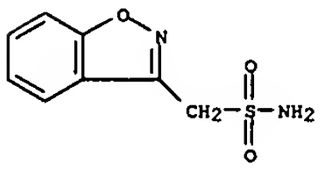
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS

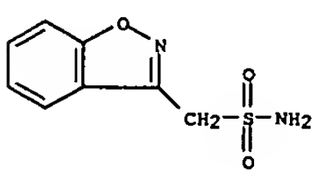
L7 ANSWER 40 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 41 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:759770 CAPLUS
DOCUMENT NUMBER: 137:15274
TITLE: Pharmacophore model for antiepileptic drugs acting on sodium channels
AUTHOR(S): Tasso, Silvina M.; Bruno-Blanch, Luis E.; Estiu, Guillermina L.
CORPORATE SOURCE: Quim. Med., Dep. de Ciencias Biol., Fac. de Ciencias Exactas, Univ. Nacional de La Plata, La Plata, 1900, Argent.
SOURCE: Journal of Molecular Modeling [online computer file] (2001), 7(7), 231-239
CODEN: JMMOFK; ISSN: 0948-5023
URL: http://link.springer.de/link/service/journals/00894/papers/1007007/10070231.pdf
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Fifteen antiepileptic drugs (AED), active against the maximal electroshock seizure test and able to block the neuronal voltage-dependent sodium channel, have been studied by a similarity anal. Structural and electronic, quantum chemical derived characteristics are compared. Rigid analogs are included, because of the flexibility of some structures, to discern the conformational requirements associated with these ligands in the moment of the interaction. An inactive compound (ethosuximide) helps in the definition of the structural factors that are important for the activity. We propose a pharmacophore model that, giving an interpretation of the biol. activity, allows the design of new AED with a well-defined mechanism of interaction.
IT 68291-97-4, Zonisamide
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(pharmacophore model for antiepileptic drugs acting on sodium channels)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



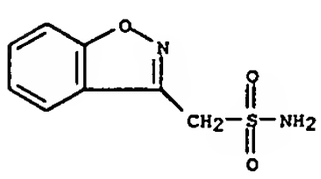
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 42 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:708976 CAPLUS
DOCUMENT NUMBER: 134:246739
TITLE: The next wave of anticonvulsants Focus on levetiracetam, oxcarbazepine and zonisamide
AUTHOR(S): Schachter, Steven C.
CORPORATE SOURCE: Department of Neurology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA
SOURCE: CNS Drugs (2000), 14(3), 229-249
CODEN: CNDREF; ISSN: 1172-7047
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 155 refs. Since Dec. 1999, 3 drugs have been cleared for marketing by the US Food and Drug Administration for the treatment of partial-onset seizures in adults with epilepsy - levetiracetam, oxcarbazepine and zonisamide. All are approved as adjunctive therapy; oxcarbazepine is also approved as monotherapy. Levetiracetam appears to have a novel mechanism of action, while the others block voltage-sensitive sodium channels (oxcarbazepine and zonisamide) and T-type calcium channels (zonisamide). Levetiracetam and oxcarbazepine have short serum elimination half-lives and can be started at therapeutic dosages. All 3 drugs exhibit linear pharmacokinetics and have a low propensity for drug-drug interactions. There is extensive worldwide experience with oxcarbazepine and zonisamide, whereas exposure to levetiracetam has been limited to a relatively small number of patients in clin. trials. These 3 drugs are important addns. to the armamentarium for the treatment of seizures and offer patients whose lives are compromised by epilepsy the potential to achieve a better quality of life.
IT 68291-97-4, Zonisamide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(levetiracetam, oxcarbazepine and zonisamide anticonvulsant therapy in humans with epilepsy)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 155 THERE ARE 155 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 43 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:682125 CAPLUS
DOCUMENT NUMBER: 134:187701
TITLE: An assessment of zonisamide as an anti-epileptic drug
AUTHOR(S): Jain, Kewal K.
CORPORATE SOURCE: Jain PharmaBiotech, Basel, CH-4057, Switz.
SOURCE: Expert Opinion on Pharmacotherapy (2000), 1(6), 1245-1260
CODEN: EOPHF7; ISSN: 1465-6566
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A brief review with 65 refs. of epilepsy as a disease, anti-epileptic drugs and methods of evaluation of anti-epileptic drugs are presented as a background for assessment of zonisamide, which has been approved by the FDA as add-on therapy for the treatment of partial seizures with or without secondary generalization in adults. Chemical, zonisamide is classified as a sulfonamide and is unrelated to other anti-epileptic drugs. The mode of action of zonisamide remains unclear, but likely mechanisms are blockade of sodium and T-type calcium channels. It is also shown to have some neuroprotective effect against hypoxia and ischemia. It has a liner pharmacokinetics with excellent oral bioavailability. Zonisamide has been approved for use in Japan for ten years prior to approval in USA and Europe. Clin. experience with zonisamide in Japan has documented its efficacy in the treatment of partial seizures (partial-onset generalized tonic-clonic, simple partial and/or complex partial seizures) and to a more variable extent, generalized tonic-clonic, generalized tonic (mainly seen in symptomatic generalized epilepsies including Lennox-Gastaut Syndrome) and compound/combination seizures. The efficacy and safety was confirmed in trials conducted in USA and Europe in adults as well as children. Zonisamide compares favorably with other newly introduced drugs and has the potential for development as a monotherapy for epilepsy.
IT 68291-97-4, Zonisamide
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(assessment of zonisamide as an antiepileptic drug)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

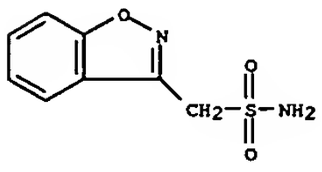
L7 ANSWER 44 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:441913 CAPLUS
DOCUMENT NUMBER: 133:68975
TITLE: Methods and ion-dependent cotransporter antagonist compounds for treating central and peripheral nervous system disorders and methods for screening the compounds
INVENTOR(S): Hochman, Daryl
PATENT ASSIGNEE(S): Cytoscan Sciences L.L.C., USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037616	A1	20000629	WO 1999-US30806	19991222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6834238	B1	20041221	US 1999-326244	19990604
CA 2356460	AA	20000629	CA 1999-2356460	19991222
AU 2000023845	A5	20000712	AU 2000-23845	19991222
EP 1141251	A1	20011010	EP 1999-967584	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002533353	T2	20021008	JP 2000-589672	19991222

PRIORITY APPLN. INFO.: US 1998-113620P P 19981223
US 1999-326244 A 19990604
US 1998-88494P P 19980608
WO 1999-US30806 W 19991222

AB Methods and compns. for treating selected conditions of the central and peripheral nervous systems employing non-synaptic mechanisms are described. Examples of the selected conditions are seizure, epilepsy, status epilepticus, migraine, spreading depression, intracranial hypertension; pathophysiol. effects of head trauma, stroke, ischemia and hypoxia; pathophysiol. effects of neurotoxic agents such as ethanol; neuropsychiatric disorders, and central nervous system edema. Treatment comprises administering agents that modulate ionic concns. and/or ionic gradients in the brain, particularly ion-dependent or cation-chloride cotransporter antagonists. Electrolyte cotransport antagonists (e.g., furosemide) and combinations of such compns. with other agents are disclosed . Methods and systems for screening drug candidate compds. for desired activities using in vitro and in vivo systems are also described.
IT **68291-97-4**, Zonisamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination with ion-dependent cotransporter antagonist; Methods and compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)
RN 68291-97-4 CAPLUS

L7 ANSWER 44 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

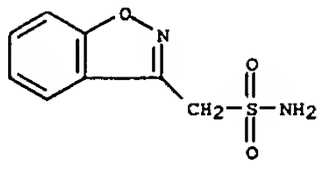


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 45 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:775041 CAPLUS
DOCUMENT NUMBER: 132:233703
TITLE: Age-related changes in the cerebral distribution of 99mTc-ECD from infancy to adulthood
AUTHOR(S): Kuji, Ichiei; Sumiya, Hisashi; Niida, Yo; Takizawa, Noboru; Ikeda, Eiji; Tsuji, Shiro; Tonami, Norihisa
CORPORATE SOURCE: Departments of Nuclear Medicine and Pediatrics, Kanazawa University, Kanazawa, Japan
SOURCE: Journal of Nuclear Medicine (1999), 40(11), 1818-1824
CODEN: JNMEAQ; ISSN: 0161-5505
PUBLISHER: Society of Nuclear Medicine, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

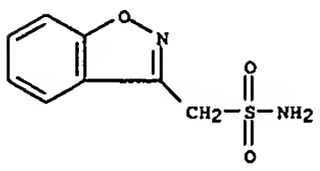
AB Although cerebral blood flow in infants differs from that in older individuals, the distribution of 99mTc-Et cysteinate dimer (ECD) in infants has not been well studied. This study compared 99mTc-ECD distribution in infants and children with that in young adults. Methods: 99mTc-ECD SPECT was performed on 37 patients suspected of having epilepsy, ranging in age from 3 mo to 26 yr. The patients were divided into two age-matched groups, a drug-free group (n = 19) and a drug-taking group (n = 18), according to their anticonvulsant medication status at the time of examination 99mTc-ECD (100-740 MBq) was injected interictally, and SPECT data were acquired using a triple-head gamma camera. Mean whole-brain counts were obtained from 10 sequential SPECT images. Regions of interest were set bilaterally on five areas of the cerebral cortex and on the basal ganglia, thalamus and cerebellum. The brain perfusion index (BPI) was obtained as a ratio of the mean counts in each region of interest to the mean whole-brain counts. The relationship between BPI and age in each region in the drug-free and drug-taking groups was analyzed sep. and together using linear regression. The relationship between five patient age groups (<1 y, n = 4; 1-4 y, n = 9; 5-9 y, n = 8; 10-15 yr, n = 7; > 15 yr, n = 9) and BPI in each region was also examined using multiple comparison analyses. Results: Significant pos. correlations between BPI and age in the frontal cortex and cerebellum were confirmed in the drug-free group. Anticonvulsant drugs did not affect the regression lines of BPI in the frontal cortex and cerebellum. Significant differences in BPI between age groups were seen in the parietal cortex, frontal cortex, occipital cortex, basal ganglia, thalamus and cerebellum in all patients. Conclusion: Age-related changes in cerebral 99mTc-ECD distribution were confirmed and found to be unaffected by the administration of anticonvulsant drugs. 99mTc-ECD uptake in children and infants is different from cerebral blood flow glucose metabolism as previously reported, especially in the cerebellum.
IT **68291-97-4**, Zonisamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(age-related changes in cerebral distribution of 99mTc-ECD from infancy to adulthood: effect of anticonvulsants)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

L7 ANSWER 45 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



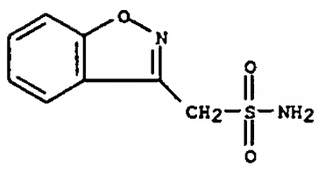
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 46 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:533154 CAPLUS
DOCUMENT NUMBER: 131:179105
TITLE: Zonisamide: a new antiepileptic drug
AUTHOR(S): Oommen, Kalarickal J.; Mathews, Sunil
CORPORATE SOURCE: Department of Neurology, Comprehensive Oklahoma Program for Epilepsy, Oklahoma University Health Sciences Center, Oklahoma City, OK, USA
SOURCE: Clinical Neuropharmacology (1999), 22(4), 192-200
CODEN: CLNEDB; ISSN: 0362-5664
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 57 refs. Zonisamide (ZNS) is a relatively new antiepileptic medication currently available in Japan. Attempts to market the drug in the United States were thwarted by reports of nephrolithiasis by European and American investigators. However, successful marketing of the drug in Japan has resulted in a renewed interest in bringing the drug to the United States. Japanese experience with ZNS showed a broad spectrum of efficacy in the treatment of seizures, including infantile spasms and myoclonic seizures. A neuro-protective role and an antimanic effect have also been reported. The exact antiepileptic mechanism of action of ZNS is not known, but it has dose-dependent sodium channel blocking and T-type calcium channel blocking properties and free radical scavenging actions. Recommended initial adult dosage in Japan is 100-200 mg/d, increased if necessary to 200-400 mg/d, up to a maximum of 600 mg/d. In children, initial dosage is 2-4 mg/kg/d, increased if necessary to 4-8 mg/kg/d up to a maximum of 12 mg/kg/d. The recommended therapeutic plasma ZNS concentration is 10-20 mg/L. Adverse events, most notably drowsiness, loss of appetite, gastrointestinal problems, and CNS toxicity, have been noted with plasma ZNS concns. of >30 mg/L. A drug rash also has been reported.
IT 68291-97-4, Zonisamide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(zonisamide, a new antiepileptic drug in humans)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



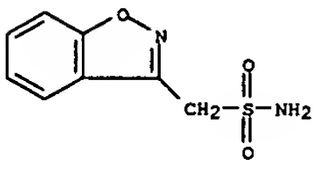
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 47 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:49593 CAPLUS
DOCUMENT NUMBER: 130:104709
TITLE: Capillary electrophoresis for therapeutic drug monitoring of antiepileptics
AUTHOR(S): Kataoka, Yasufumi; Makino, Kazutaka; Oishi, Ryozo
CORPORATE SOURCE: Dep. Hospital Pharmacy, Fac. Medicine, Kyushu Univ., Fukuoka, 812, Japan
SOURCE: Electrophoresis (1998), 19(16-17), 2856-2860
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB The authors examined the use of capillary electrophoresis for therapeutic drug monitoring of antiepileptic drugs. Micellar electrokinetic capillary chromatog. (MEKC) with a diode array detector simultaneously determined concns. of zonisamide, a new type of antiepileptic drug, and phenobarbital, phenytoin and carbamazepine, typical antiepileptic drugs, in human serum. Zonisamide levels in human serum obtained by MEKC correlated well with levels obtained by high-performance liquid chromatog. The serum levels of phenobarbital, phenytoin and carbamazepine determined by MEKC were almost equal to those obtained by fluorescence polarization immunoassay. The reproducibility of separation and quantification with MEKC for intra- and inter-day assays were appropriate. This MEKC method could provide a simple and efficient therapeutic drug monitoring method for antiepileptic drugs, especially in patients treated with a combination of zonisamide and other antiepileptic drugs. MEKC may be an attractive method for therapeutic drug monitoring, because of its specificity of separation, automation of procedure, ease of method development, low cost, small aqueous buffer amts., speed of anal., small injection volume and high environment-directed performance. A review is added.
IT 68291-97-4, Zonisamide
RL: ANT (Analyte); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(capillary electrophoresis for therapeutic drug monitoring of antiepileptics)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



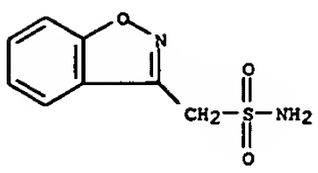
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 48 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:10158 CAPLUS
DOCUMENT NUMBER: 130:20184
TITLE: Metabolic fate of clobazam. VII. Interactions between clobazam and typical antiepileptic drugs. I
AUTHOR(S): Arimoto, Masahiro; Kato, Kumi; Nishitani, Tomoko; Yokoyama, Nobuharu; Yoshida, Yoichi; Koike, Kazuhiro
CORPORATE SOURCE: Research Labs., Nippon Shoji Kaisha, Ltd., Ibaraki, 567, Japan
SOURCE: Iyakuhin Kenkyu (1997), 28(6), 477-489
CODEN: IYKEDH; ISSN: 0287-0894
PUBLISHER: Nippon Koteisho Kyokai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB The drug interaction between clobazam (CLB) and each of 7 typical antiepileptic drugs (AEDs) in rats and dogs was studied following single and consecutive oral administrations. 1) Effects of CLB on the serum levels of typical AEDs in rats. The serum levels of valproic acid (VPA), ethosuximide (ESM) and phenobarbital (PB) were significantly decreased by single oral co-administration of CLB. The effects of CLB on the serum levels of typical AEDs were similar in single and consecutive co-administration. 2) Effects of typical AEDs on CLB and M-9 plasma levels in rats. The plasma CLB and M-9 levels were significantly decreased by single oral co-administration of ESM (500 mg/kg). The plasma levels of CLB and M-9, as well as M-9/CLB ratio, were significantly affected by consecutive oral co-administration of typical AEDs except for VPA (100 mg/kg). 3) Effect of CLB on the serum levels of VPA and effect of VPA on CLB and M-9 plasma levels after consecutive oral administration in dogs. AUC of CLB was not significantly decreased with treatment of co-administration. AUC values of VPA and M-9 were significantly decreased with treatment of co-administration.
IT 68291-97-4, Zonisamide
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolic fate of clobazam. VII. Interactions between clobazam and typical antiepileptic drugs. I)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



L7 ANSWER 49 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:805674 CAPLUS
DOCUMENT NUMBER: 130:191299
TITLE: Clinical pharmacology and therapeutic drug monitoring of zonisamide
AUTHOR(S): Mimaki, Takashi
CORPORATE SOURCE: Department of Special Needs Education, Faculty of Education, Gifu University, Gifu, Japan
SOURCE: Therapeutic Drug Monitoring (1998), 20(6), 593-597
CODEN: TDMODV; ISSN: 0163-4356
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 30 refs. Zonisamide (1,2-benzisoxazole-3-methanesulfonamide) is a new antiepileptic drug developed in Japan. This compound is insol. in water, and it is available in tablet and powder form.
In exptl. animals, this compound has been found to have a strong inhibitory effect on convulsions of cortical origin because it suppresses focal spiking and the spread of secondary generalized seizures. In humans, a series of double-blind, placebo-controlled studies revealed the efficacy of zonisamide for patients with refractory partial seizures and for selected patients with infantile spasms. Its antiepileptic mechanism of action remains unclear, but it is likely to involve blockade of both sodium and T-type calcium channels. Oral bioavailability of zonisamide is excellent in healthy human volunteers. Zonisamide is slowly absorbed and has a mean tmax of 5 to 6 h. Almost 100% of it is absorbed; there is no difference in bioavailability between tablets and powder. Zonisamide concns. are highest in erythrocytes and then in whole blood and plasma. It is approx. 40% to 60% bound to plasma proteins, primarily albumin. Its volume distribution is 0.9 to 1.4 L/kg. In adults, the elimination half-life is between 50 and 62 h, and it takes as long as 2 wk to reach steady state. The dose-serum level correlation is linear up to doses of 10 to 15 mg/kg per day, and the therapeutic range is 10 to 40 μg/mL. However, the relationship between serum zonisamide levels, clin. response, and adverse effects appears weak. Concurrent enzyme-inducing anticonvulsants such as phenytoin, carbamazepine, or barbiturates stimulate zonisamide metabolism and decrease serum zonisamide levels at steady state. Although zonisamide has been reported to increase the serum levels of phenytoin and carbamazepine in some patients, the interactions of zonisamide with other antiepileptic drugs seem to be of minor clin. relevance. A pilot study of zonisamide suppositories revealed that it is beneficial for patients with neurol. disorders in whom antiepileptic drugs cannot be administered by mouth.
IT 68291-97-4, Zonisamide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(clin. pharmacol. and therapeutic drug monitoring of zonisamide in humans)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

L7 ANSWER 49 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
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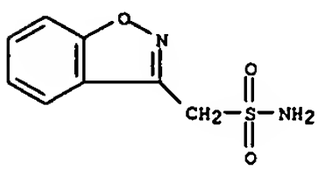
L7 ANSWER 50 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:623530 CAPLUS
DOCUMENT NUMBER: 129:339807
TITLE: Lamotrigine inhibits monoamine uptake in vitro and modulates 5-hydroxytryptamine uptake in rats
AUTHOR(S): Southam, Eric; Kirkby, Debbie; Higgins, Guy A.; Hagan, Russell M.
CORPORATE SOURCE: Neuroscience Unit, Glaxo Wellcome Medicines Research Centre, Herts, Stevenage, SG1 2NY, UK
SOURCE: European Journal of Pharmacology (1998), 358(1), 19-24
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lamotrigine is a novel anticonvulsant drug which also stabilizes mood in bipolar illness via an unknown mechanism. We report the concentration-dependent inhibition of 5-hydroxytryptamine (5-HT) uptake in both human platelets and rat brain synaptosomes (IC50s were 240 and 474 μM, resp.) by lamotrigine. Synaptosomal uptake of noradrenaline (IC50 239 μM) and dopamine (IC50 322 μM) was also inhibited. Tetrodotoxin failed to modulate 5-HT uptake suggesting that sodium channel blockade does not mediate the lamotrigine effect. Lithium, sodium valproate, zonisamide, and carbamazepine all possess anti-manic activity but only the latter inhibited 5-HT uptake. The inhibition of the p-chloroamphetamine-induced 5-HT syndrome in rats suggests that lamotrigine also inhibits 5-HT uptake in vivo. These effects probably reflect an affinity for biogenic amine transporters. However, at present, it remains uncertain whether, at clin. EDs, these effects contribute significantly to the efficacy of lamotrigine in bipolar illness.
IT 68291-97-4, Zonisamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(lamotrigine inhibits monoamine uptake in vitro and modulates 5-hydroxytryptamine uptake in rats)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 51 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:523407 CAPLUS
DOCUMENT NUMBER: 129:269819
TITLE: Cellular mechanisms for felbamate, stiripentol, tiagabine, vigabatrin and zonisamide
AUTHOR(S): Monaco, Francesco
CORPORATE SOURCE: Department of Neurosciences, University of Torino, Italy
SOURCE: Current Problems in Epilepsy (1997), 12(Molecular and Cellular Targets for Antiepileptic Drugs), 207-213
CODEN: CPEPES; ISSN: 0950-4591
PUBLISHER: John Libbey & Co. Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 29 refs. (1) Vigabatrin (γ-vinyl-GABA) (GVG) is a relatively specific irreversible inhibitor of GABA-T, the major enzyme responsible for the catabolic degradation of GABA in the mammalian CNS. Administration of GVG to laboratory exptl. animals produces a prolonged inhibition of brain GABA-T, with a concomitant elevation in whole brain GABA concns., more evident in the synaptosomal pool. The results of a variety of pharmacol. studies demonstrated that GVG is effective in a number of models in which alterations of GABAergic neurotransmission play a significant role, i.e. epilepsy, analgesia, spasticity and tardive dyskinesia. (2) The precise mechanism of action of felbamate (2-phenyl-1,3-propanediol dicarbamate) (FLB) is not known, but it specifically interacts at the strychnine-insensitive glycine recognition site on the NMDA receptor-ionophore complex. It also affects significantly sodium flux in vitro similar to other AEDs. Recent studies suggest a dual action on excitatory and inhibitory GABA-mediated brain mechanisms. (3) Information on the neuropharmacol. action of the allylic acid stiripentol (STP) is limited. It increases brain GABA concns. by inhibition of its synaptosomal uptake or by decreasing its metabolic turnover, with a mechanism of action different from that of valproic acid. (4) Tiagabine (TGB), a nipecotic acid derivative, acts by inhibiting GABA re-uptake by glial cells and presynaptic neurons. (5) As zonisamide (ZNS) (1,2-benzioxazole-3-methanesulfonamide) has a sulfamoyl group in common with acetazolamide (AZA), it was suspected that its anticonvulsant activity could be related to a an inhibitory effect on carbonic anhydrase (CA). However, ZNS is 100 times less potent in vitro and 100-1000 times less potent ex vivo than AZA. Recent studies have demonstrated that the drug blocks voltage-sensitive sodium and calcium channels, so disrupting over-synchronized neuronal firing and subsequent epileptic activity.
IT 68291-97-4, Zonisamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(cellular anticonvulsant mechanisms for felbamate, stiripentol, tiagabine, vigabatrin and zonisamide)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

L7 ANSWER 51 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 52 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

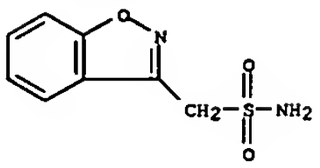
ACCESSION NUMBER: 1997:601406 CAPLUS
DOCUMENT NUMBER: 127:288005
TITLE: Zonisamide as a neuroprotective agent in an adult gerbil model of global forebrain ischemia: a histological, in vivo microdialysis and behavioral study
AUTHOR(S): Owen, Andrew J.; Ijaz, Sadiq; Miyashita, Hiro; Wishart, Tom; Howlett, Wendy; Shuaib, Ashfaq
CORPORATE SOURCE: Saskatchewan Stroke Research Centre, University of Saskatchewan, Saskatoon, Can.
SOURCE: Brain Research (1997), 770(1,2), 115-122
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Brief periods of global cerebral ischemia are known to produce characteristic patterns of neuronal injury both in human studies and in exptl. animal models. Ischemic damage to vulnerable areas such as the CA1 sector of the hippocampus is thought to result from excitotoxic amino acid neurotransmission. The objective of this study was to determine the ability of a novel sodium channel blocking compound, zonisamide, to reduce neuronal damage by preventing the ischemia-associated accumulation of extracellular glutamate. Using a gerbil model, animals were subjected to 5 min ischemic insults. Both pre- and post-ischemic drug administration (zonisamide 150 mg/kg) were studied. Histol. brain sections were prepared using a silver stain at 7 and 28 days post ischemia. The animals sacrificed at 28 days also underwent behavioral testing using a modified Morris water maze. In vivo microdialysis was performed on a sep. group of animals in order to determine the patterns of ischemia-induced glutamate accumulation in the CA1 sector of the hippocampus. Pyramidal cell damage scores in the CA1 region of the hippocampus were significantly reduced in animals pre-treated with zonisamide compared to saline-treated controls, both at 7 days and 28 days post ischemia. However, animals receiving zonisamide post-treatment did not display significant differences from controls. Behavioral studies also showed significant preservation of function in drug-treated animals. Microdialysis studies confirmed a reduction in glutamate release in drug-treated animals compared to saline-treated controls. Our data suggest that zonisamide is effective in reducing neuronal damage by a mechanism involving decreased ischemia-induced extracellular glutamate accumulation and interruption of excitotoxic pathways.

IT 68291-97-4, Zonisamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(zonisamide as a neuroprotective agent in an adult gerbil model of global forebrain ischemia)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

L7 ANSWER 52 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 53 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

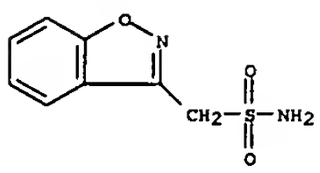
ACCESSION NUMBER: 1996:501993 CAPLUS
DOCUMENT NUMBER: 125:157510
TITLE: The clinical pharmacokinetics of the newer antiepileptic drugs: Focus on topiramate, zonisamide and tiagabine
AUTHOR(S): Perucca, Emilio; Bialer, Meir
CORPORATE SOURCE: Department Internal Medicine and Therapeutics, University Pavia, Pavia, Italy
SOURCE: Clinical Pharmacokinetics (1996), 31(1), 29-46
CODEN: CPKNDH; ISSN: 0312-5963
PUBLISHER: Adis
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 120 refs. Following the introduction of felbamate, gabapentin, lamotrigine, oxcarbazepine and vigabatrin in the early 1990s, other new antiepileptic drugs have been advancing in clin. development. Those most extensively evaluated to date include topiramate, zonisamide and tiagabine. Topiramate, licensed recently in the UK, acts multifactorially through the blockade of sodium channels and kainate/AMPA receptors, enhancement of γ-aminobutyric acid (GABA)ergic transmission and inhibition of carbonic anhydrase. It is well absorbed from the gastrointestinal tract and negligibly bound to plasma proteins. When used as a monotherapy, topiramate is eliminated primarily in the urine in an unchanged form with a half-life of 20 to 30 h; elimination is faster in patients receiving concurrent medication with enzyme-inducing anticonvulsants, in whom the extent of biotransformation becomes more prominent. Zonisamide, which has been com. available in Japan for some years, also has a multifactorial mode of action, possibly involving the blockade of sodium channels, T-type calcium channels and inhibition of carbonic anhydrase. It is rapidly absorbed, 50% bound to plasma proteins and is eliminated predominantly by biotransformation; zonisamide has a half-life of 50 to 70 h in monotherapy patients, or 25 to 35 h in patients comedicated with enzyme-inducing anticonvulsants. Tiagabine, a nipecotic acid derivative which inhibits GABA reuptake, is rapidly and completely absorbed after oral intake. It is highly (96%) bound to plasma proteins and it is eliminated primarily by cytochrome P 450 3A-mediated oxidation, with a half-life of about 7 h in healthy volunteers. Tiagabine metabolism is also enhanced by concurrent medication with enzyme-inducing anticonvulsants, resulting in a need to use dosages larger than those required in monotherapy or valproic acid (sodium valproate)-treated patients. Addnl. investigational antiepileptic agents included in this article are rufinamide (CGP 33101), fosphenytoin, levetiracetam, losigamone, remacemide and stiripentol. All these drugs have undergone early characterization with respect to pharmacokinetic features and interaction potential.

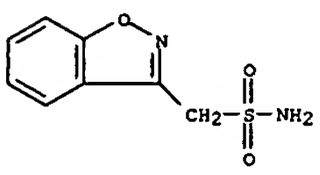
IT 68291-97-4, Zonisamide
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(clin. pharmacokinetics of the newer antiepileptic drugs, which are topiramate, zonisamide and tiagabine in humans)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

L7 ANSWER 53 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

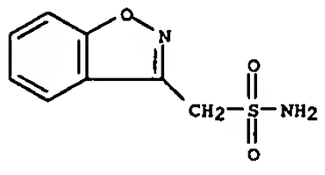


L7 ANSWER 57 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:16160 CAPLUS
DOCUMENT NUMBER: 118:16160
TITLE: Effects of antiepileptic drugs on sodium channel in rat brain
AUTHOR(S): Tamai, Hiroshi; Mimaki, Takashi; Ogihara, Tohru; Mino, Makoto
CORPORATE SOURCE: Dep. Pediatr., Osaka Med. Coll., Takatsuki, Japan
SOURCE: Japanese Journal of Psychiatry and Neurology (1992), 46(2), 544-5
CODEN: JJPNEA; ISSN: 0912-2036
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Voltage-sensitive sodium channels mediate increases in Na+ permeability that are responsible for the rising phase of the action potential in neutrons. Both diphenylhydantoin (PHT) and carbamazepine (CBZ) have proven to decrease the early, transient sodium currents in mammalian myelinated nerve fibers. In the present study, the authors examined the effects of antiepileptic drugs on the sodium channel by measuring [3H]saxitoxin (SAX) binding to the rat brain membrane preparation Preincubation with 0.1 mM PHT inhibited the specific [3H]SAX binding to the brain membrane preparation of 23.2 ± 2.0% of control. On the other hand, no effect was seen on the specific [3H]SAX binding by pretreatment with CBZ, valproate phenobarbitol of zonisamide. This inhibition of PHT was reversible since the decreased specific [3H]SAX binding was recovered after washing out PHT from the incubation medium.
IT 68291-97-4, Zonisamide
RL: BIOL (Biological study)
(brain sodium channels response to)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

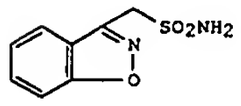


L7 ANSWER 58 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

L7 ANSWER 58 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:210875 CAPLUS
DOCUMENT NUMBER: 112:210875
TITLE: Effects of antiepileptic drugs on benzodiazepine and GABA receptors in rat brain
AUTHOR(S): Mimaki, Takashi; Suzuki, Yasuhiro; Tagawa, Tetsuzo
CORPORATE SOURCE: Med. Sch., Osaka Univ., Osaka, 553, Japan
SOURCE: Shinkei Kenkyu no Shinpo (1989), 33(6), 899-908
CODEN: SKNSAF; ISSN: 0001-8724
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Benzodiazepine and GABA receptors possess several pharmacol. important roles since there is a good correlation between anxiolytic, anticonvulsant, or muscle-relaxant activity and benzodiazepine and GABA receptor binding. The effects of phenobarbital (PB), sodium valproate (VPA), carbamazepine (CBZ), phenytoin (PHT), diazepam (DZP), clonazepam (CZP), zonisamide (ZNS), and γ-vinyl-GABA on specific [3H]flunitrazepam and [3H]muscimol binding were studied in Sprague-Dawley rat brain. Specific flunitrazepam binding was almost completely displaced by 10-4-10-6M DZP and CZP, and was decreased to 74.9%, 68.2%, and 91.9% of control values by 10-4M CBZ, PHT, and ZNS, resp. Specific muscimol binding was decreased to 68.3%, and 87.8% by 10-4M ZNS and γ-vinyl-GABA, resp. There were 11.3%, 31.1%, and 30.3% increases in benzodiazepine receptor d. (Bmax) caused by i.p. injection of 100 and 500 mg/kg VPA and 50 mg/kg ZNS, resp. Since ZNS displaced binding of label from both benzodiazepine and GABA receptors, a study of ZNS binding was undertaken in rat brain. [3H]ZNS bound in a saturable fashion to the crude synaptosomal fraction of whole rat brain. Displacement studies revealed an inhibitory effect of CZP, and an enhancement effect of GABA and secobarbital, on specific ZNS binding. The regional distribution study of specific ZNS binding sites revealed sites similar to GABA receptors. These results suggest that specific ZNS binding sites have a high correlation with the GABA-benzodiazepine receptor-ionophore complex in the synaptic membrane. The effects of γ-vinyl-GABA on the GABA receptor-coupled Cl- channel were studied. Preincubation of brain synaptoneurosomes with therapeutic concns. of γ-vinyl-GABA (100-1000 μM), as well as GABA, produced a reversible concentration-dependent decrease in net 36Cl- uptake, which suggests desensitization of the GABA receptor-coupled Cl- channel.
IT 68291-97-4, Zonisamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(benzodiazepine and GABAergic receptors of brain response to)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

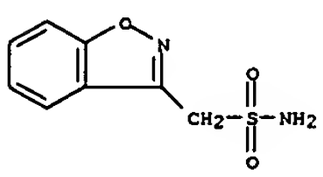


L7 ANSWER 59 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:225336 CAPLUS
DOCUMENT NUMBER: 110:225336
TITLE: Blockade of sustained repetitive action potentials in cultured spinal cord neurons by zonisamide (AD 810, CI 912), a novel anticonvulsant
AUTHOR(S): Rock, David M.; Macdonald, Robert L.; Taylor, Charles P.
CORPORATE SOURCE: Dep. Pharmacol., Warner-Lambert Co., Ann Arbor, MI, 48105, USA
SOURCE: Epilepsy Research (1989), 3(2), 138-43
CODEN: EPIRE8; ISSN: 0920-1211
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

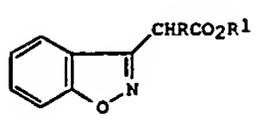


I

AB Zonisamide (I) (≥3 μg/mL) blocked the sustained firing of action potentials induced by depolarizing steps of current injection across the membrane of intracellularly recorded mouse spinal cord neurons. Responses to GABA and glutamate were not altered by zonisamide, and spontaneously synaptically evoked activity was not reduced until higher concns. of zonisamide (10 μg/mL) were applied. Thus, the anticonvulsant and neurol. side effects of zonisamide appear to be unrelated to modulation of GABA or glutamate receptors. The anticonvulsant action of zonisamide can be accounted for by a selective action on voltage-dependent sodium channels of neurons, as has been proposed for other anticonvulsants.
IT 68291-97-4, Zonisamide
RL: BIOL (Biological study)
(spinal cord neurotransmission response to, as anticonvulsant, side effects in relation to)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



L7 ANSWER 60 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:610931 CAPLUS
DOCUMENT NUMBER: 109:210931
TITLE: Novel base-induced reactions of substituted (1,2-benzisoxazol-3-yl)acetic acid esters
AUTHOR(S): Ueda, Shozo; Naruto, Shunsuke; Yoshida, Toyokichi; Sawayama, Tadahiro; Uno, Hitoshi
CORPORATE SOURCE: Res. Lab., Dainippon Pharm. Co., Ltd., Osaka, 564, Japan
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1988), (5), 1013-21
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 109:210931
GI



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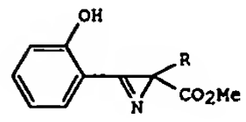
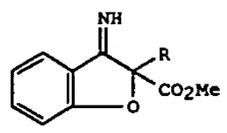
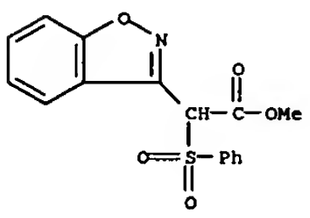


II



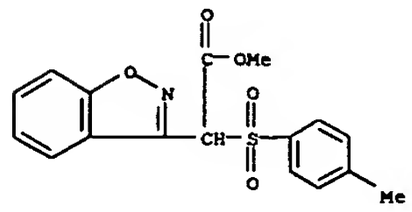
III

AB Me benzisoxazolylacetates I (R = Me, CH2Ph, cyclohexyl, OPh, SPh, R1 = Me)
reacted with NaH, Me3COK, or MeONa in DMF to give 60-91% azirines II, whereas I (R = NMe2, morpholino, hexahydro-1H-azepinyl, 4-phenylpiperazinyl, R1 = Me) gave 45-76% iminobenzofurans III. Under the
same conditions I (R = Br, Cl, R1 = Me) dimerized to give a mixture of (E)-
and (Z)-MeO2CCR2:CR2CO2Me (R2 = 1,2-benzisoxazol-3-yl).
IT 117375-35-6P 117375-36-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and attempted reaction with sodium hydride)
RN 117375-35-6 CAPLUS
CN 1,2-Benzisoxazole-3-acetic acid, α-(phenylsulfonyl)-, methyl ester (9CI) (CA INDEX NAME)

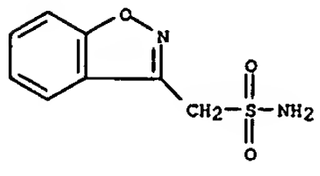


L7 ANSWER 60 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 117375-36-7 CAPLUS
CN 1,2-Benzisoxazole-3-acetic acid, α-[(4-methylphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)



L7 ANSWER 61 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:451938 CAPLUS
DOCUMENT NUMBER: 107:51938
TITLE: Zonisamide enhances slow sodium inactivation in Myxicola
AUTHOR(S): Schauf, C. L.
CORPORATE SOURCE: Dep. Biol., Indiana Univ., Indianapolis, IN, 46223, USA
SOURCE: Brain Research (1987), 413(1), 185-8
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In voltage-clamped Myxicola giant axons Zonisamide caused a hyperpolarizing shift in the steady-state fast inactivation curve and retarded recovery from fast and slow Na+ inactivation. The effects of Zonisamide on steady-state fast inactivation could be described assuming a
single binding site with a dissociation constant of 12 μM. Slow inactivation
was significantly more sensitive, with a Kd of 1 μM from both steady-state and kinetic data. While these results account for anticonvulsant activity, the differential sensitivity suggests Zonisamide may also be useful in studies of the slow inactive state of the Na+ channel.
IT 68291-97-4, Zonisamide
RL: BIOL (Biological study)
(slow sodium inactivation in Myxicola by, in sodium channel characterization)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



L7 ANSWER 62 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1980:453966 CAPLUS
DOCUMENT NUMBER: 93:53966
TITLE: 3-(Sulfamoylmethyl)-1,2-benzisoxazole as an anticonvulsant
INVENTOR(S): Uno, Jun; Kurokawa, Mikio; Masuda, Yoshinobu
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 54163823	A2	19791226	JP 1978-71377	19780612
JP 61059288	B4	19861216		

PRIORITY APPLN. INFO.: JP 1978-71377 A 19780612

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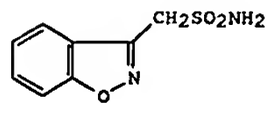
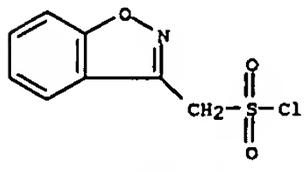


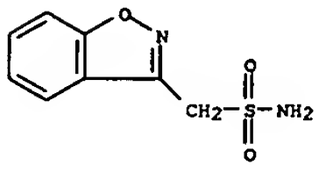
I

AB Anticonvulsants contained 3-(sulfamoylmethyl)-1,2-benzisoxazole (I) [68291-97-4] or its alkali salts as major components. Thus, a tablet composition contained I 100, lactose 35, starch 17, crystalline cellulose 40,
poly(vinylpyrrolidone) 6, silicic anhydride 1, and Mg stearate 1 g, which showed ED50 of 11.9 mg/kg against maximum elec. shock in rats, vs. 18.0 mg/kg
for diphenylhydantoin (II) and carbamazepine (III). The LD50 for I, II, and III were 1829, 363, and 1700 mg/kg p.o. resp.
IT 73101-65-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amination of)
RN 73101-65-2 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonyl chloride (9CI) (CA INDEX NAME)

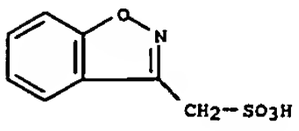


IT 68291-97-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP

L7 ANSWER 62 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(Preparation); USES (Uses)
(prepn. and anticonvulsant activity of)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

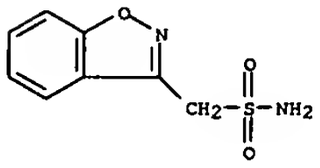


IT 73101-64-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with phosphoryl chloride)
RN 73101-64-1 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, sodium salt (9CI) (CA INDEX NAME)



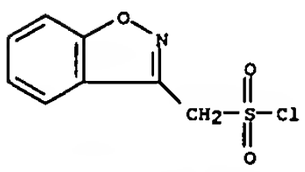
● Na

IT 68291-98-5P
RL: PREP (Preparation)
(preparation of, as anticonvulsant)
RN 68291-98-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, monosodium salt (9CI) (CA INDEX NAME)

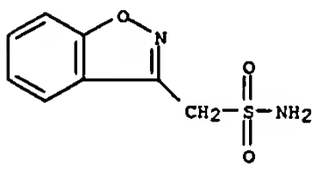


● Na

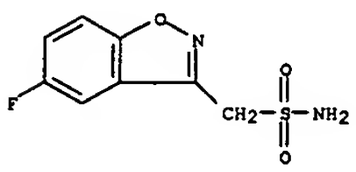
L7 ANSWER 63 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(prepn. and amidation of)
RN 73101-65-2 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonyl chloride (9CI) (CA INDEX NAME)



IT 68291-97-4P 68291-99-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and anticonvulsant activity of)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



RN 68291-99-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-fluoro- (9CI) (CA INDEX NAME)



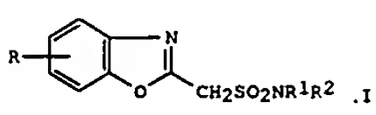
IT 68292-02-4P 68292-03-5P 68292-05-7P
68292-06-8P 68292-07-9P 68292-08-0P
68292-10-4P 68292-12-6P 68292-13-7P
68292-14-8P 68292-16-0P 68292-17-1P
68292-18-2P 68292-19-3P 68292-20-6P
68936-37-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antispasmodic activity of)
RN 68292-02-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-methyl- (9CI) (CA INDEX NAME)

L7 ANSWER 63 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1980:408158 CAPLUS
DOCUMENT NUMBER: 93:8158
TITLE: Heterocyclic methanesulfonamide derivatives with anticonvulsive action
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: Fr. Demande, 23 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

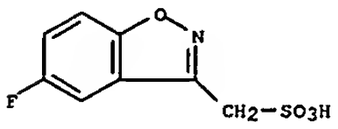
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2428033	A1	19800104	FR 1978-17345	19780609
FR 2428033	B1	19801121		

PRIORITY APPLN. INFO.: FR 1978-17345 A 19780609

OTHER SOURCE(S): MARPAT 93:8158
GI



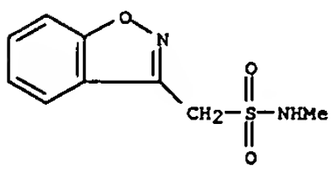
AB 2-Benzoxazolemethanesulfonamides and benzisoxazole isomers I and II [R = H, halo; R1 and R2 (same or different) are H or alkyl], which were prepared
from the bromoethyl analogs, showed anticonvulsant and antispasmodic activity. 3-(Bromomethyl)benzisoxazole reacted with Na2SO3, the Na methanesulfonate analog obtained was converted to the acid chloride, and the product was treated with NH3 to give II (R = R1 = R2 = H).
IT 73535-64-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of)
RN 73535-64-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, 5-fluoro-, sodium salt (9CI) (CA INDEX NAME)



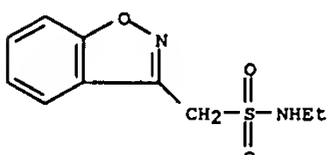
● Na

IT 73101-65-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

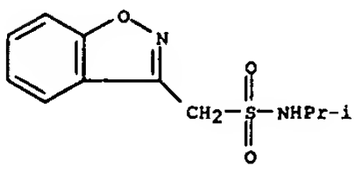
L7 ANSWER 63 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



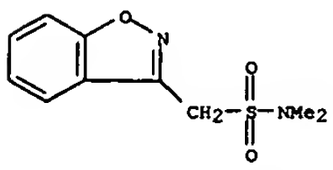
RN 68292-03-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-ethyl- (9CI) (CA INDEX NAME)



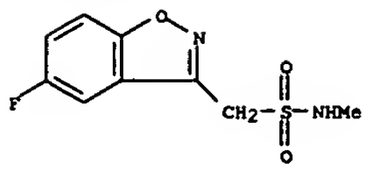
RN 68292-05-7 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-(1-methylethyl)- (9CI) (CA INDEX NAME)



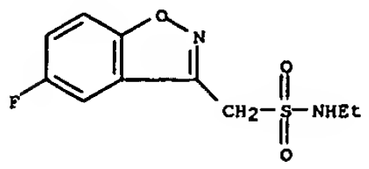
RN 68292-06-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N,N-dimethyl- (9CI) (CA INDEX NAME)



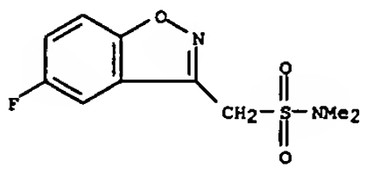
RN 68292-07-9 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-fluoro-N-methyl- (9CI) (CA INDEX NAME)



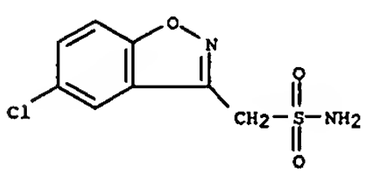
RN 68292-08-0 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-ethyl-5-fluoro- (9CI) (CA INDEX NAME)



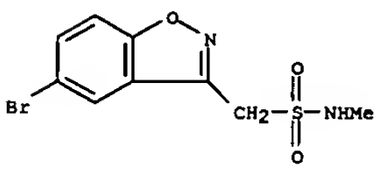
RN 68292-10-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-fluoro-N,N-dimethyl- (9CI) (CA INDEX NAME)



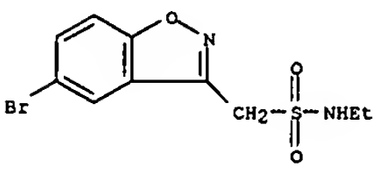
RN 68292-12-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-chloro- (9CI) (CA INDEX NAME)



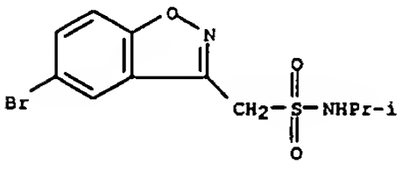
RN 68292-13-7 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-chloro-N-methyl- (9CI) (CA INDEX NAME)



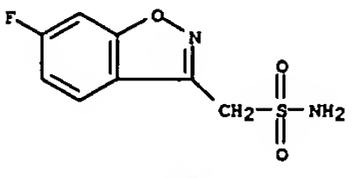
RN 68292-19-3 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-bromo-N-ethyl- (9CI) (CA INDEX NAME)



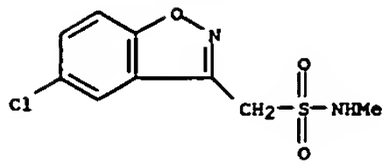
RN 68292-20-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-bromo-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



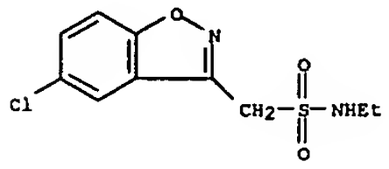
RN 68936-37-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 6-fluoro- (9CI) (CA INDEX NAME)



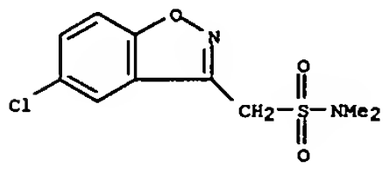
IT 73101-64-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with phosphoryl chloride)
RN 73101-64-1 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, sodium salt (9CI) (CA INDEX NAME)



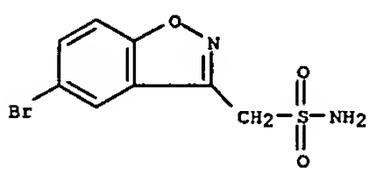
RN 68292-14-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-chloro-N-ethyl- (9CI) (CA INDEX NAME)



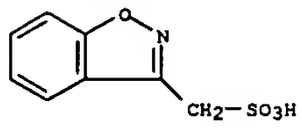
RN 68292-16-0 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-chloro-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 68292-17-1 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-bromo- (9CI) (CA INDEX NAME)

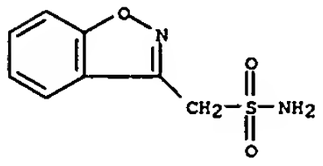


RN 68292-18-2 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-bromo-N-methyl- (9CI) (CA INDEX NAME)



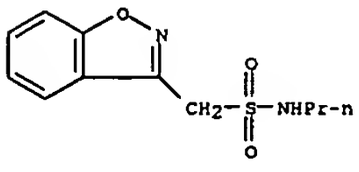
● Na

IT 68291-98-5P 68292-04-6P 68292-09-1P
68292-15-9P 68292-21-7P 73101-76-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 68291-98-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, monosodium salt (9CI) (CA INDEX NAME)

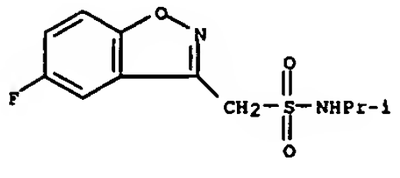


● Na

RN 68292-04-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-propyl- (9CI) (CA INDEX NAME)

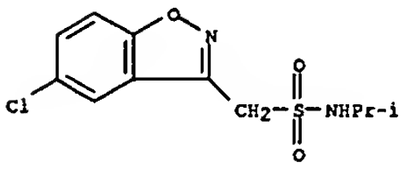


RN 68292-09-1 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-fluoro-N-(1-methylethyl)- (9CI) (CA INDEX NAME)

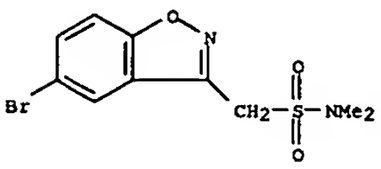


L7 ANSWER 63 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

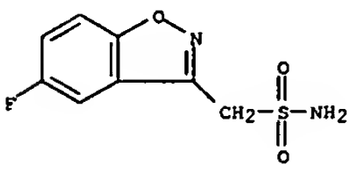
RN 68292-15-9 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-chloro-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 68292-21-7 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-bromo-N,N-dimethyl- (9CI) (CA INDEX NAME)

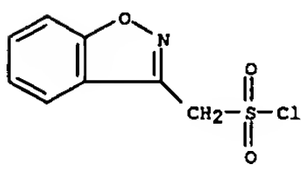


RN 73101-76-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-fluoro-, monosodium salt (9CI) (CA INDEX NAME)

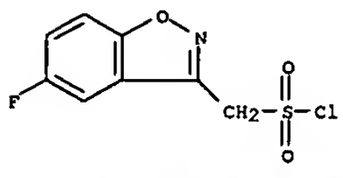


● Na

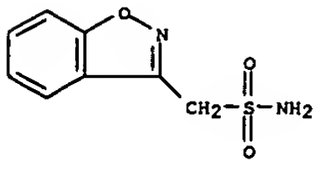
L7 ANSWER 64 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 73101-65-2 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonyl chloride (9CI) (CA INDEX NAME)



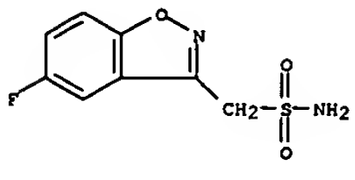
RN 73101-66-3 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonyl chloride, 5-fluoro- (9CI) (CA INDEX NAME)



IT **68291-97-4P 68291-99-6P 68292-02-4P**
68292-03-5P 68292-04-6P 68292-06-8P
68292-07-9P 68292-08-0P 68292-10-4P
68292-13-7P 68292-14-8P 68292-16-0P
68292-17-1P 68292-18-2P 68292-19-3P
68292-20-6P 68936-37-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and anticonvulsant properties of)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



RN 68291-99-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-fluoro- (9CI) (CA INDEX NAME)

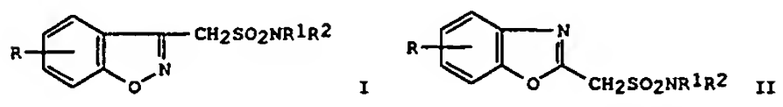


L7 ANSWER 64 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1980:181160 CAPLUS
DOCUMENT NUMBER: 92:181160
TITLE: Methane-sulfonamide derivatives
INVENTOR(S): Uno, Hitoshi; Kurokawa, Mikio; Masuda, Yoshinobu
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

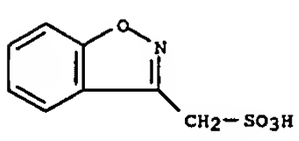
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4172896	A	19791030	US 1978-912857	19780605
PRIORITY APPLN. INFO.:			US 1978-912857 A	19780605

OTHER SOURCE(S): MARPAT 92:181160
GI



AB Benzisoxazole- and benzoxazolemethanesulfonamides I and II [R = H, halo; R1, R2 (same or different) = H, C1-3 alkyl], useful as anticonvulsants, were prepared Thus, stirring 3-(bromomethyl)-1,2-benzisoxazole in MeOH with aqueous NaSO3 at 50° 4 h gave Na 1,2-benzisoxazole-3-methanesulfonate, which was converted to the acid chloride with POCl3 and treated with NH3 to give I (R = H). I and II had activity similar to that of diphenylhydantoin but with about twice the safety index.

IT **73101-64-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and acid chloride formation from)
RN 73101-64-1 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, sodium salt (9CI) (CA INDEX NAME)

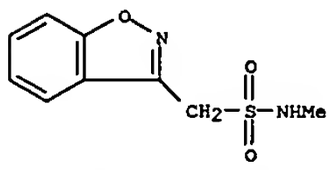


● Na

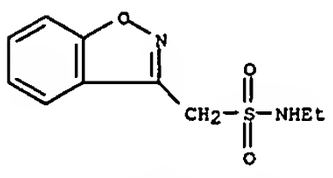
IT **73101-65-2P 73101-66-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and ammonolysis of)

L7 ANSWER 64 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

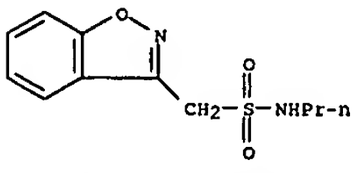
RN 68292-02-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-methyl- (9CI) (CA INDEX NAME)



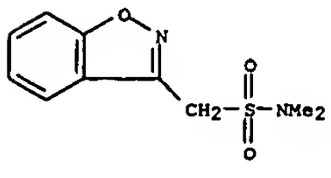
RN 68292-03-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-ethyl- (9CI) (CA INDEX NAME)



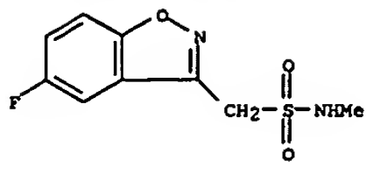
RN 68292-04-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-propyl- (9CI) (CA INDEX NAME)



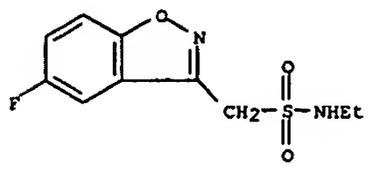
RN 68292-06-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N,N-dimethyl- (9CI) (CA INDEX NAME)



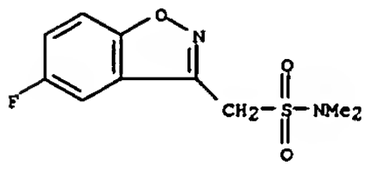
RN 68292-07-9 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-fluoro-N-methyl- (9CI) (CA INDEX NAME)



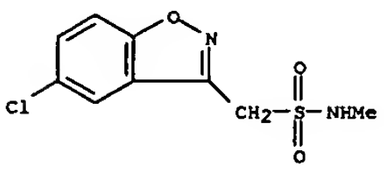
RN 68292-08-0 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-ethyl-5-fluoro- (9CI) (CA INDEX NAME)



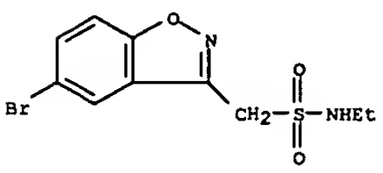
RN 68292-10-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-fluoro-N,N-dimethyl- (9CI) (CA INDEX NAME)



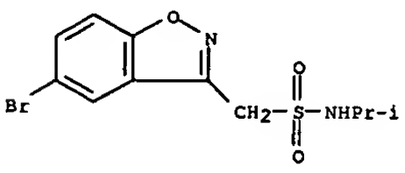
RN 68292-13-7 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-chloro-N-methyl- (9CI) (CA INDEX NAME)



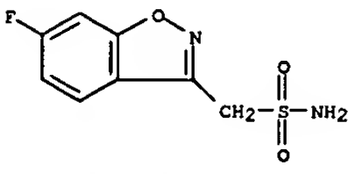
RN 68292-14-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-chloro-N-ethyl- (9CI) (CA INDEX NAME)



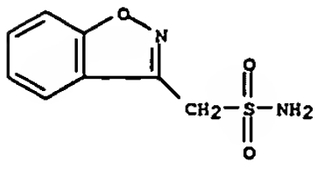
RN 68292-20-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-bromo-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



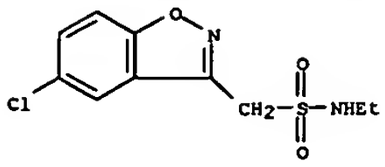
RN 68936-37-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 6-fluoro- (9CI) (CA INDEX NAME)



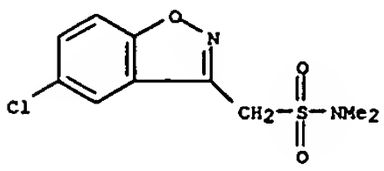
IT **68291-98-5P 68292-05-7P 68292-09-1P**
68292-12-6P 68292-15-9P 68292-21-7P
73101-76-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 68291-98-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, monosodium salt (9CI) (CA INDEX NAME)



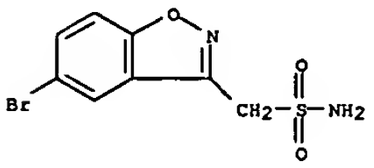
● Na



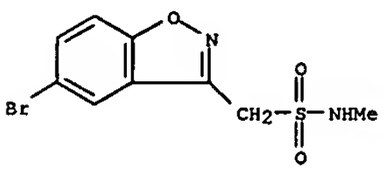
RN 68292-16-0 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-chloro-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 68292-17-1 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-bromo- (9CI) (CA INDEX NAME)

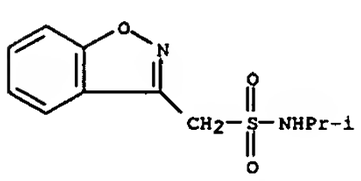


RN 68292-18-2 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-bromo-N-methyl- (9CI) (CA INDEX NAME)

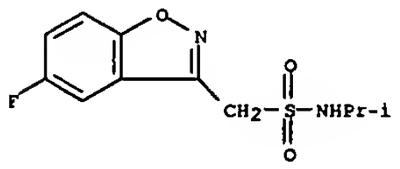


RN 68292-19-3 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-bromo-N-ethyl- (9CI) (CA INDEX NAME)

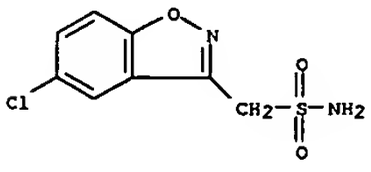
RN 68292-05-7 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-(1-methylethyl)- (9CI) (CA INDEX NAME)



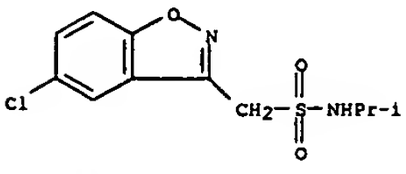
RN 68292-09-1 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-fluoro-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 68292-12-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-chloro- (9CI) (CA INDEX NAME)

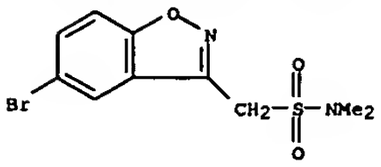


RN 68292-15-9 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-chloro-N-(1-methylethyl)- (9CI) (CA INDEX NAME)

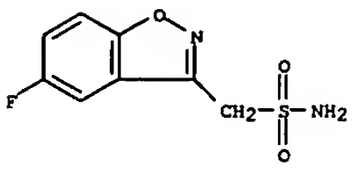


RN 68292-21-7 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-bromo-N,N-dimethyl- (9CI) (CA INDEX NAME)

L7 ANSWER 64 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

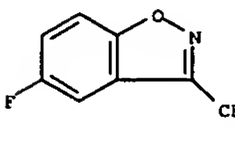


RN 73101-76-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-fluoro-, monosodium salt (9CI) (CA INDEX NAME)



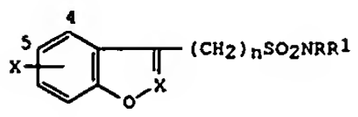
● Na

IT 73535-64-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phosphorus oxychloride)
RN 73535-64-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, 5-fluoro-, sodium salt (9CI) (CA INDEX NAME)



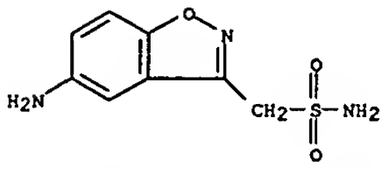
● Na

L7 ANSWER 65 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:66514 CAPLUS
DOCUMENT NUMBER: 90:66514
TITLE: Studies on 3-substituted 1,2-benzisoxazole derivatives. 6. Syntheses of 3-(sulfamoylmethyl)-1,2-benzisoxazole derivatives and their anticonvulsant activities
AUTHOR(S): Uno, Hitoshi; Kurokawa, Mikio; Masuda, Yoshinobu; Nishimura, Haruki
CORPORATE SOURCE: Res. Lab., Dainippon Pharm. Co., Ltd., Suita, Japan
SOURCE: Journal of Medicinal Chemistry (1979), 22(2), 180-3
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 90:66514
GI



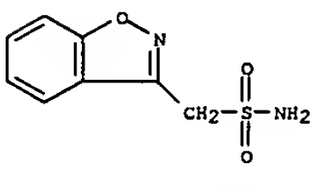
I

AB Forty-three 3-(sulfamoylmethyl)-1,2-benzisoxazole [68291-97-4] derivs. I (NRR1 = NH2, NHMe, NHNH2, etc.; X = H, F, Cl, Br, etc.; n = 1, 2, or 3) were synthesized and tested for anticonvulsant activity in mice. Most of I were synthesized from 3-(bromomethyl)-1,2-benzisoxazole [37924-85-9] by reaction with Na2SO3 followed by chlorination and amination. When X = halogen at position 5 of I, increased activity and neurotoxicity was observed I (R = R1 = X = H, n = 1) [68291-97-4] was the most promising anticonvulsant. Structure-activity relations are discussed.
IT 68936-39-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acetylation of)
RN 68936-39-0 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-amino- (9CI) (CA INDEX NAME)

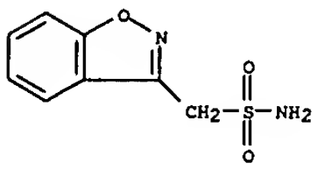


IT 68291-97-4DP, derivs. 68291-97-4P 68291-99-6P
68292-01-3P 68292-02-4P 68292-03-5P
68292-04-6P 68292-05-7P 68292-06-8P
68292-07-9P 68292-08-0P 68292-09-1P
68292-10-4P 68292-11-5P 68292-12-6P
68292-13-7P 68292-14-8P 68292-15-9P
68292-16-0P 68292-17-1P 68292-18-2P
68292-19-3P 68292-20-6P 68292-21-7P

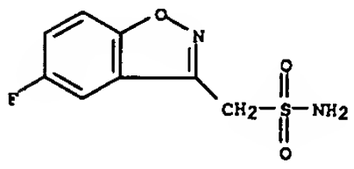
L7 ANSWER 65 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
68292-22-8P 68357-44-8P 68936-23-2P
68936-24-3P 68936-25-4P 68936-26-5P
68936-27-6P 68936-28-7P 68936-29-8P
68936-30-1P 68936-31-2P 68936-32-3P
68936-33-4P 68936-34-5P 68936-35-6P
68936-36-7P 68936-37-8P 68936-38-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and anticonvulsant activity of)
RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

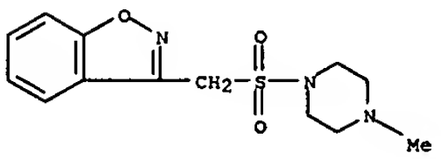


RN 68291-99-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-fluoro- (9CI) (CA INDEX NAME)

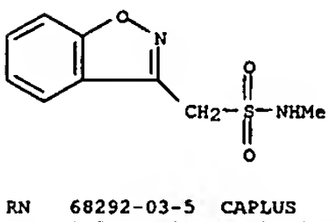


RN 68292-01-3 CAPLUS
CN Piperazine, 1-[(1,2-benzisoxazol-3-ylmethyl)sulfonyl]-4-methyl- (9CI) (CA INDEX NAME)

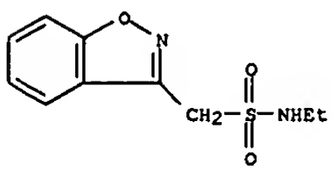
L7 ANSWER 65 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



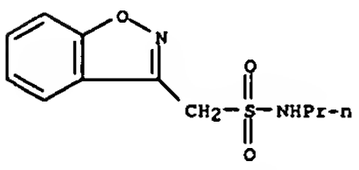
RN 68292-02-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-methyl- (9CI) (CA INDEX NAME)



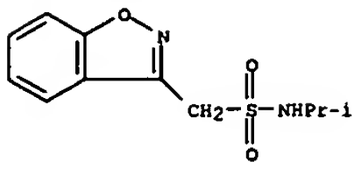
RN 68292-03-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-ethyl- (9CI) (CA INDEX NAME)



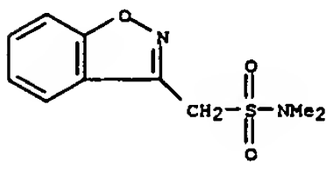
RN 68292-04-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-propyl- (9CI) (CA INDEX NAME)



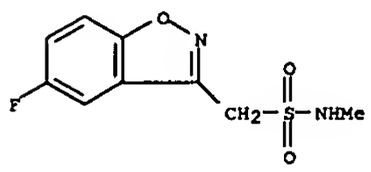
RN 68292-05-7 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-(1-methylethyl)- (9CI) (CA INDEX NAME)



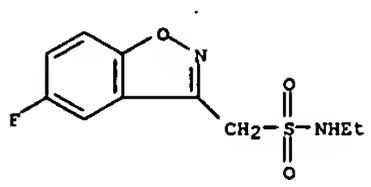
RN 68292-06-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N,N-dimethyl- (9CI) (CA INDEX NAME)



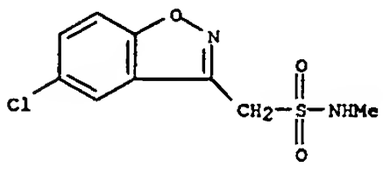
RN 68292-07-9 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-fluoro-N-methyl- (9CI) (CA INDEX NAME)



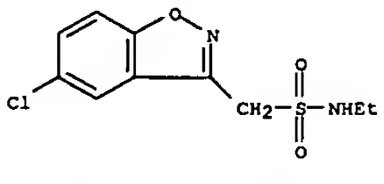
RN 68292-08-0 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-ethyl-5-fluoro- (9CI) (CA INDEX NAME)



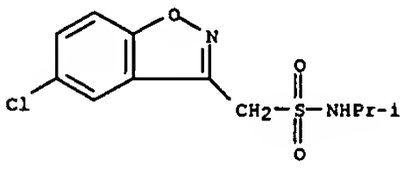
RN 68292-09-1 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-fluoro-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



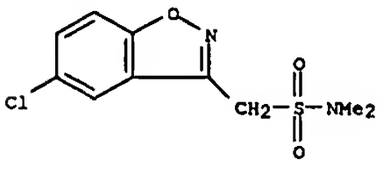
RN 68292-14-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-chloro-N-ethyl- (9CI) (CA INDEX NAME)



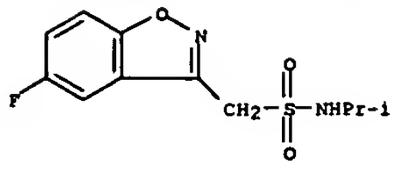
RN 68292-15-9 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-chloro-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



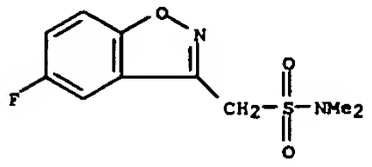
RN 68292-16-0 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-chloro-N,N-dimethyl- (9CI) (CA INDEX NAME)



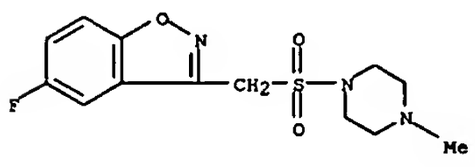
RN 68292-17-1 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-bromo- (9CI) (CA INDEX NAME)



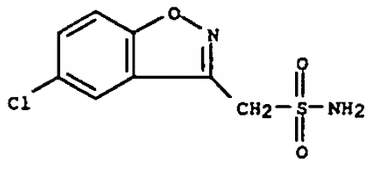
RN 68292-10-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-fluoro-N,N-dimethyl- (9CI) (CA INDEX NAME)



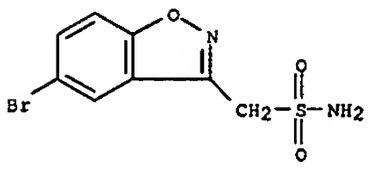
RN 68292-11-5 CAPLUS
CN Piperazine, 1-[[(5-fluoro-1,2-benzisoxazol-3-yl)methyl]sulfonyl]-4-methyl- (9CI) (CA INDEX NAME)



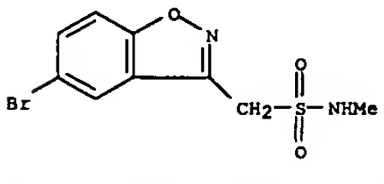
RN 68292-12-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-chloro- (9CI) (CA INDEX NAME)



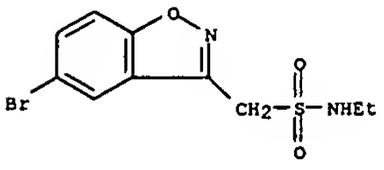
RN 68292-13-7 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-chloro-N-methyl- (9CI) (CA INDEX NAME)



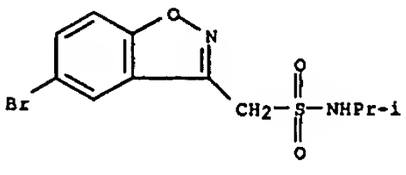
RN 68292-18-2 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-bromo-N-methyl- (9CI) (CA INDEX NAME)



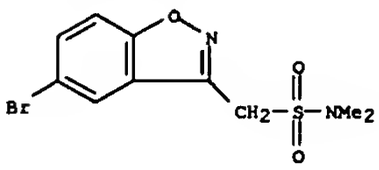
RN 68292-19-3 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-bromo-N-ethyl- (9CI) (CA INDEX NAME)



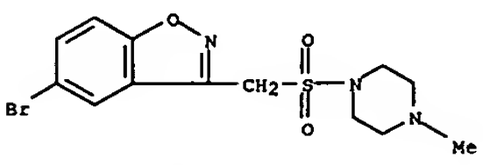
RN 68292-20-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-bromo-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



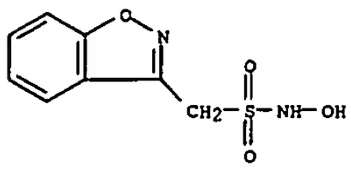
RN 68292-21-7 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-bromo-N,N-dimethyl- (9CI) (CA INDEX NAME)



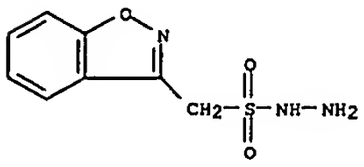
RN 68292-22-8 CAPLUS
CN Piperazine, 1-[[(5-bromo-1,2-benzisoxazol-3-yl)methyl]sulfonyl]-4-methyl- (9CI) (CA INDEX NAME)



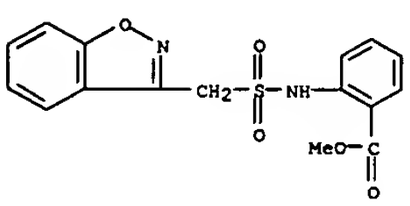
RN 68357-44-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-hydroxy- (9CI) (CA INDEX NAME)



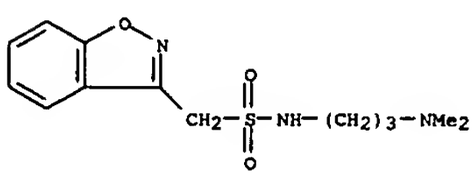
RN 68936-23-2 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, hydrazide (9CI) (CA INDEX NAME)



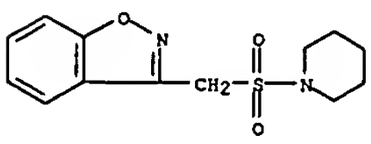
RN 68936-24-3 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonic acid, 2,2-dimethylhydrazide (9CI) (CA INDEX NAME)



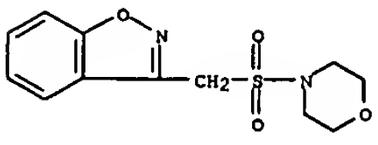
RN 68936-29-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



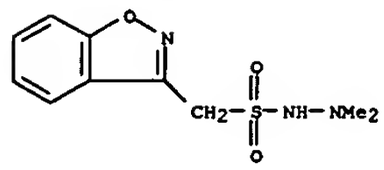
RN 68936-30-1 CAPLUS
CN Piperidine, 1-[(1,2-benzisoxazol-3-ylmethyl)sulfonyl]- (9CI) (CA INDEX NAME)



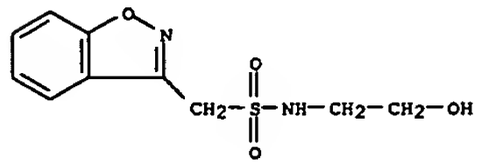
RN 68936-31-2 CAPLUS
CN Morpholine, 4-[(1,2-benzisoxazol-3-ylmethyl)sulfonyl]- (9CI) (CA INDEX NAME)



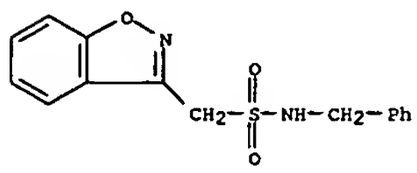
RN 68936-32-3 CAPLUS
CN Piperazine, 1-[(1,2-benzisoxazol-3-ylmethyl)sulfonyl]-4-phenyl- (9CI) (CA INDEX NAME)



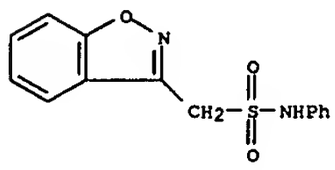
RN 68936-25-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



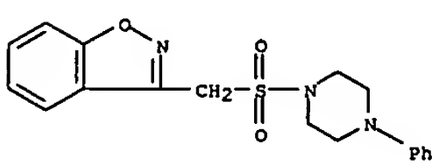
RN 68936-26-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-(phenylmethyl)- (9CI) (CA INDEX NAME)



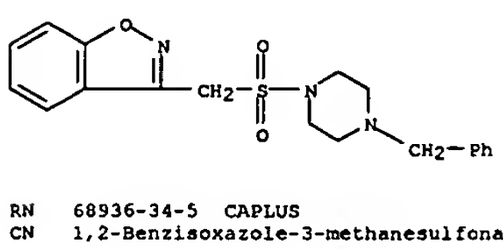
RN 68936-27-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-phenyl- (9CI) (CA INDEX NAME)



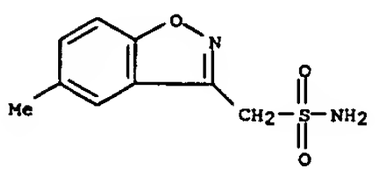
RN 68936-28-7 CAPLUS
CN Benzoic acid, 2-[[[(1,2-benzisoxazol-3-ylmethyl)sulfonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



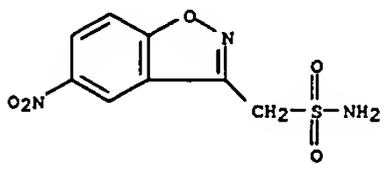
RN 68936-33-4 CAPLUS
CN Piperazine, 1-[(1,2-benzisoxazol-3-ylmethyl)sulfonyl]-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



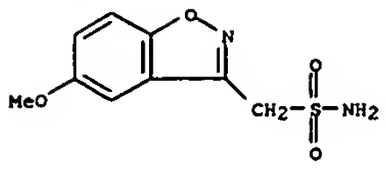
RN 68936-34-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-methyl- (9CI) (CA INDEX NAME)



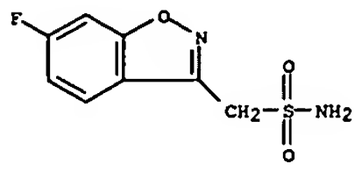
RN 68936-35-6 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-nitro- (9CI) (CA INDEX NAME)



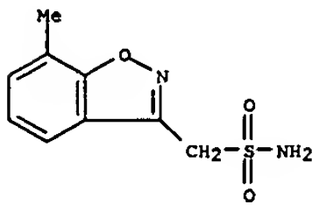
RN 68936-36-7 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 5-methoxy- (9CI) (CA INDEX NAME)



RN 68936-37-8 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 6-fluoro- (9CI) (CA INDEX NAME)

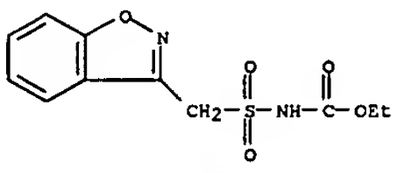


RN 68936-38-9 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, 7-methyl- (9CI) (CA INDEX NAME)



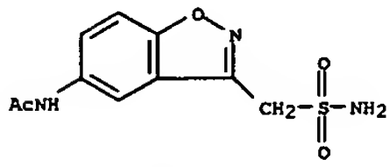
IT 68936-41-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with ammonia)

RN 68936-41-4 CAPLUS
CN Carbamic acid, [(1,2-benzisoxazol-3-ylmethyl)sulfonyl]-, ethyl ester (9CI)
(CA INDEX NAME)

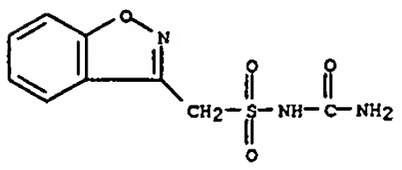


IT 68936-40-3P 68936-42-5P 68936-43-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

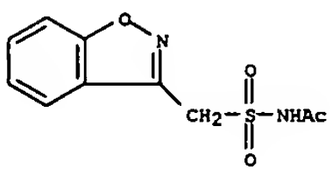
RN 68936-40-3 CAPLUS
CN Acetamide, N-[3-[(aminosulfonyl)methyl]-1,2-benzisoxazol-5-yl]- (9CI) (CA
INDEX NAME)



RN 68936-42-5 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide, N-(aminocarbonyl)- (9CI) (CA INDEX NAME)



RN 68936-43-6 CAPLUS
CN Acetamide, N-[(1,2-benzisoxazol-3-ylmethyl)sulfonyl]- (9CI) (CA INDEX NAME)



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	335.02	518.77

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-48.75	-48.75

STN INTERNATIONAL LOGOFF AT 10:11:42 ON 01 MAR 2006

L7 ANSWER 54 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

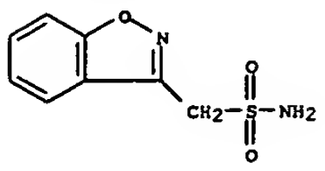
ACCESSION NUMBER: 1996:370880 CAPLUS
DOCUMENT NUMBER: 125:95793
TITLE: Pharmaceutical evaluation of 10% phenytoin powders
AUTHOR(S): Kagawa, Yoshiyuki; Sasaki, Kaori; Matsushima, Mikio; Inagaki, Shoji; Kojima, Michio
CORPORATE SOURCE: Sch. Med., Mie Univ. Sch., Tsu, 514, Japan
SOURCE: Byoin Yakugaku (1996), 22(2), 149-158
CODEN: BYYADW; ISSN: 0389-9098
PUBLISHER: Nippon Byoin Yakugakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB A dispensing test of 10% phenytoin powders (10% DPH), which has the same bioavailability as the tablet, was investigated. Pharmaceutical characteristics including an apparent d., a dispersibility, grouping properties and an angle of repose of 10% DPH passed the criteria for dispensing from the hospital pharmacy. Next, according to clin. formulas, we designed the eight standard formulas that consisting of 10% DPH with 10% phenobarbital powders, zonisamide powders, carbamazepine granules, sodium valproate granules and lactomin (Biofermin) powders. Pharmaceutical characteristics of these standard formulas also passed the criteria required for dispensing from the hospital pharmacy. The particle size of some standard formulas showed twin-peak distribution patterns. In the mixing test of the standard formulas, all of the coeffs. of variation (CV) of the phenytoin content were under 5% which met the criterion (6.1%) of a guideline of dispensing (9th Revised Edition) by Japanese Pharmacist Association CV values of net weight and phenytoin content after dividing and packing the standard formulas also met the criterion of the guideline for dispensing. The CV values of the net weight and phenytoin content in formulas exhibiting twin-peak distribution patterns in particle size were not significantly larger than those in formulas exhibiting single-peak distribution patterns of drug particles. This distribution patterns did not demonstrate a relationship to the distribution of net weight in dividing and packaging powder mixts. The CV values of the phenytoin content showed low values (<5%) independent of the particle distribution of the formulas. These results indicate that the 10% DPH has been distributed uniformly in the mixture with the other powders and that it is an useful preparation for clin. use.

IT 68291-97-4, Zonisamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of phenytoin powders)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)

L7 ANSWER 54 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



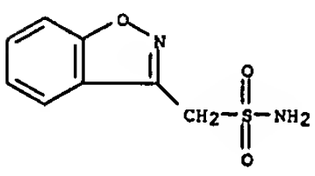
L7 ANSWER 55 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:440922 CAPLUS
DOCUMENT NUMBER: 122:234046
TITLE: Purification and characterization of cytochrome P450 3A enzyme from hepatic microsomes of untreated doguera baboons
AUTHOR(S): Ohmori, Shigeru; Kudo, Sanae; Nakasa, Hiromitsu; Horie, Toru; Kitada, Mitsukazu
CORPORATE SOURCE: Division of Pharmacy, Chiba University Hospital, Chiba, 260, Japan
SOURCE: Biological & Pharmaceutical Bulletin (1994), 17(12), 1584-8
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We isolated a form of cytochrome P 450 (P 450) from hepatic microsomes of untreated doguera baboons. The final preparation (referred to as P 450 BLa) was apparently homogeneous, as judged by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. The estimated min. mol. weight of P 450 BLa was 50 kDa. The N-terminal amino acid sequence of P 450 BLa (identified 10 residues) was identical with that of P 450 3A8 purified from cynomolgus monkeys. This protein was cross-reactive with antibodies raised against P 450 3A4 and P 450 CMLc which were P 450 3A enzymes purified from hepatic microsomes of humans and cynomolgus monkeys, resp. P 450 BLa was capable of catalyzing testosterone 6β-hydroxylation and zonisamide reduction P 450 BLa antibody inhibited the activity of testosterone 6β-hydroxylase, but not the activities of testosterone 16α- and 16β-hydroxylases in liver microsomes of doguera baboons. From these lines of evidence we conclude that P 450 BLa can be classified as part of the P 450 3A subfamily and acts as a constitutive testosterone 6β-hydroxylase in hepatic microsomes of doguera baboons.

IT 68291-97-4, Zonisamide
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(substrate; cytochrome P 450 3A enzyme purification and characterization from hepatic microsomes of doguera baboons)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)



L7 ANSWER 56 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:621704 CAPLUS
DOCUMENT NUMBER: 121:221704
TITLE: Effects of zonisamide on neurotransmitter in the mouse brain.
AUTHOR(S): Endoh, A.; Kinno, I.; Kawai, M.; Hiramatsu, M.; Mori, A.
CORPORATE SOURCE: Institute Molecular and Cellar Medicine, Okayama University Medical School, Okayama, 700, Japan
SOURCE: Neurosciences (Okayama, Japan) (1994), 20(SUPPL.), P173-P176
CODEN: NUOCDO; ISSN: 0388-7448
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Zonisamide (3-sulfamoylmethyl-1,2-benzisozazole sodium salt), an anticonvulsant, is known to inhibit either behavioral epileptic seizures or epileptic discharges in EEG induced by elec. stimulation or chemical convulsants. In the present study, we examined the effects of zonisamide on release of aspartic acid and γ -aminobutyric acid (GABA) from brain slices of the El-mouse, a genetic model for human temporal lobe epilepsy. El-mice aged about 20 wk were used. Tissue slices (0.3mm) of hippocampus were prepared using a McIlwain tissue chopper and [3H]-aspartic acid and [3H]-GABA release stimulated by high K+ was measured according to the method by Janjua et al. Results indicated that zonisamide accelerated GABA release from hippcampal tissue dose-dependently, though no effect was observed on aspartic acid release. This result suggests that a part of suppressive effects of zonisamide on epilepsy may be related to enhancement of GABAergic nerve system, which is a principal inhibitory mechanism in the brain.

IT 68291-97-4, Zonisamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zonisamide effect on GABA and aspartic acid release in hippocampus)

RN 68291-97-4 CAPLUS
CN 1,2-Benzisoxazole-3-methanesulfonamide (9CI) (CA INDEX NAME)